Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13	FEB 26	MEDLINE reloaded with enhancements
NEWS 14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
NEWS 20	MAR 20	MARPAT now updated daily
NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 26	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 28	MAY 01	New CAS web site launched
NEWS 29	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 30	MAY 11	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS EXPRESS		NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS LOGIN		Welcome Banner and News Items
NEWS IPC8		For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:50:30 ON 14 MAY 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:50:50 ON 14 MAY 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 MAY 2007 HIGHEST RN 934672-05-6
DICTIONARY FILE UPDATES: 13 MAY 2007 HIGHEST RN 934672-05-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

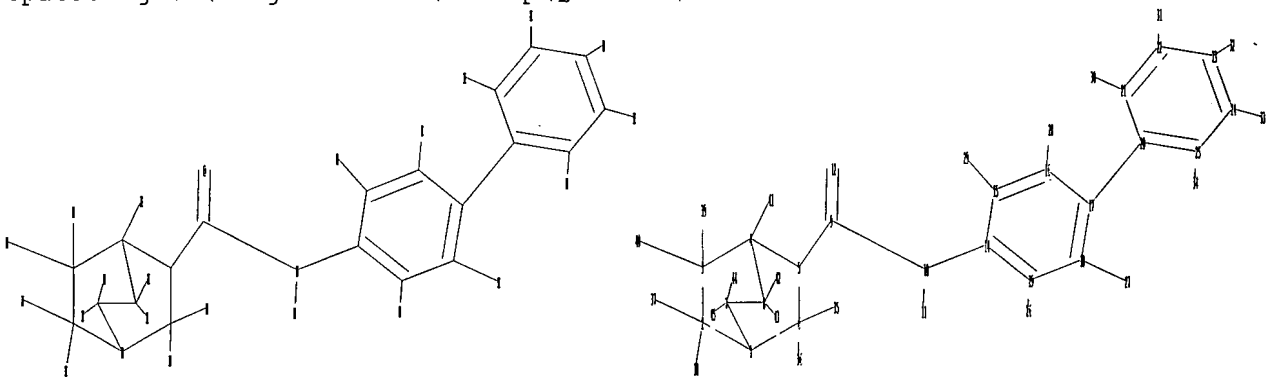
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10565181.str



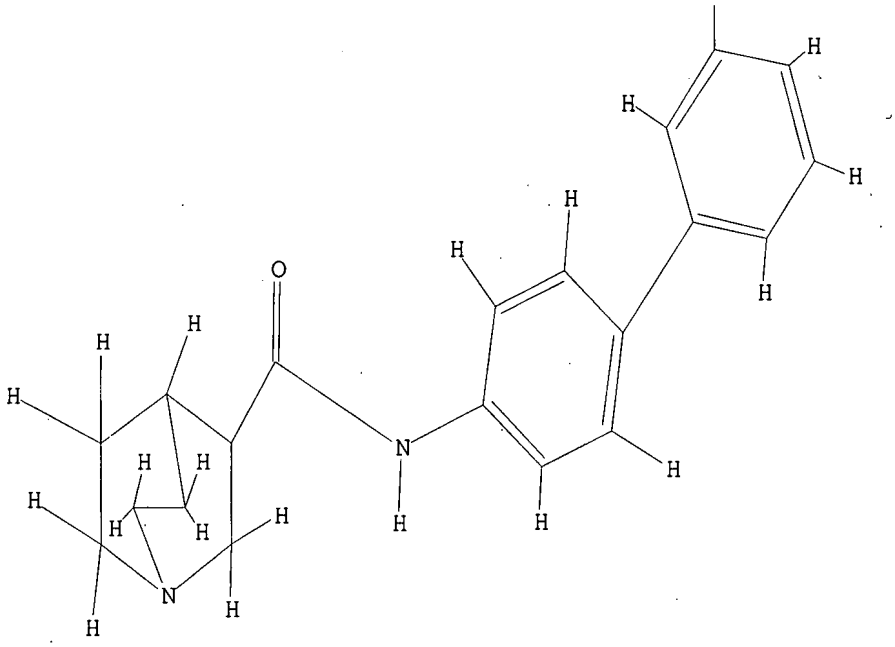
chain nodes :
9 10 11 12 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45
ring nodes :
1 2 3 4 5 6 7 8 14 15 16 17 18 19 20 21 22 23 24 25
chain bonds :
2-37 2-38 3-39 3-40 4-41 5-9 6-35 6-36 7-44 7-45 8-42 8-43 9-10 9-12 10-11 10-14 15-29 16-28 17-20 18-27 19-26 21-30 22-31 23-32 24-33 25-34

ring bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 14-15 14-19 15-16 16-17 17-18
18-19 20-21 20-25 21-22 22-23 23-24 24-25
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 9-10 9-12 10-14
exact bonds :
2-37 2-38 3-39 3-40 4-41 5-9 6-35 6-36 7-44 7-45 8-42 8-43 10-11 15-29
16-28 17-20 18-27 19-26 21-30 22-31 23-32 24-33 25-34
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19 20-21 20-25 21-22 22-23 23-24 24-25
isolated ring systems :
containing 1 : 14 : 20 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS
38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 09:51:54 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

```
FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:             7 TO      298
PROJECTED ANSWERS:                0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 09:51:58 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      165 TO ITERATE

100.0% PROCESSED      165 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L3            0 SEA SSS FUL L1

=> log y
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     172.55     172.76

STN INTERNATIONAL LOGOFF AT 09:52:03 ON 14 MAY 2007
```

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
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NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
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NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS LOGIN		Welcome Banner and News Items
NEWS IPC8		For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:55:56 ON 14 MAY 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:56:11 ON 14 MAY 2007
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STRUCTURE FILE UPDATES: 13 MAY 2007 HIGHEST RN 934672-05-6
DICTIONARY FILE UPDATES: 13 MAY 2007 HIGHEST RN 934672-05-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

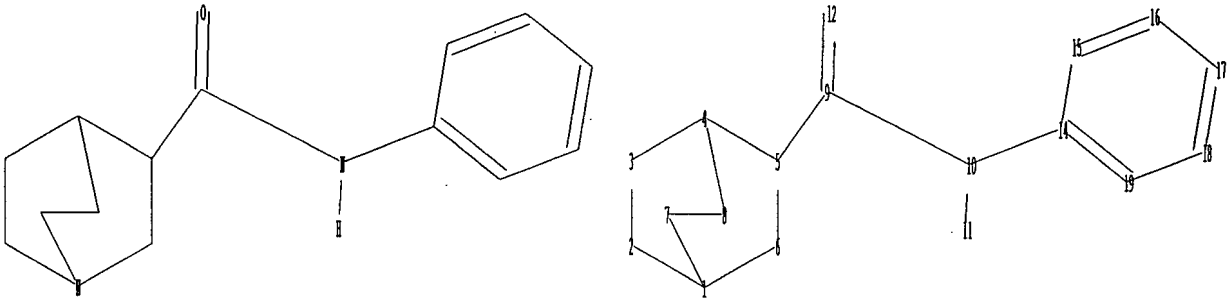
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10565181a.str



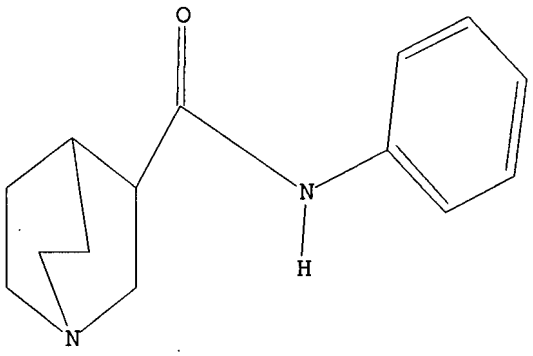
chain nodes :
9 10 11 12
ring nodes :
1 2 3 4 5 6 7 8 14 15 16 17 18 19
chain bonds :
5-9 9-10 9-12 10-11 10-14
ring bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 14-15 14-19 15-16 16-17 17-18
18-19
exact/norm bonds :
1-2 1-6 1-7 2-3 3-4 4-5 4-8 5-6 7-8 9-10 9-12 10-14
exact bonds :

5-9 10-11
normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19
isolated ring systems :
containing 1 : 14 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

L1   STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1   STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 09:56:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   366 TO ITERATE

100.0% PROCESSED   366 ITERATIONS   3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 6173 TO   8467
PROJECTED ANSWERS: 3 TO   162

L2   3 SEA SSS SAM L1

=> sl1 full
SL1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l1 full
FULL SEARCH INITIATED 09:56:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   7468 TO ITERATE

100.0% PROCESSED   7468 ITERATIONS   79 ANSWERS
SEARCH TIME: 00.00.01

```
L3            79 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     172.10     172.31

FILE 'CAPLUS' ENTERED AT 09:56:54 ON 14 MAY 2007
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FILE COVERS 1907 - 14 May 2007  VOL 146 ISS 21
FILE LAST UPDATED: 13 May 2007  (20070513/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3 full
L4            13 L3

=> d ibib abs hitstr tot

L4   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:120928  CAPLUS
DOCUMENT NUMBER:          142:198251
TITLE:                    Preparation of quinuclidine N-biarylamides for use in
                          treatment and/or prophylaxis of diseases
INVENTOR(S):              Flessner, Timo; Boess, Frank-Gerhard; Hafner,
                          Frank-Thorsten; Luithle, Joachim; Methfessel,
                          Christoph; Telan, Leila
PATENT ASSIGNEE(S):       Bayer Healthcare AG, Germany
SOURCE:                   PCT Int. Appl., 51 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ----------------     ----   --------    ---------------------    --------
     WO 2005012299         A1    20050210    WO 2004-EP8037           20040719
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10334724	A1	20050224	DE 2003-10334724	20030730
CA 2534003	A1	20050210	CA 2004-2534003	20040719
EP 1651645	A1	20060503	EP 2004-741132	20040719
EP 1651645	B1	20070221		
R: DE, ES, FR, GB, IT				
JP 2007500152	T	20070111	JP 2006-521462	20040719

PRIORITY APPLN. INFO.: DE 2003-10334724 A 20030730
WO 2004-EP8037 W 20040719

OTHER SOURCE(S): CASREACT 142:198251; MARPAT 142:198251

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

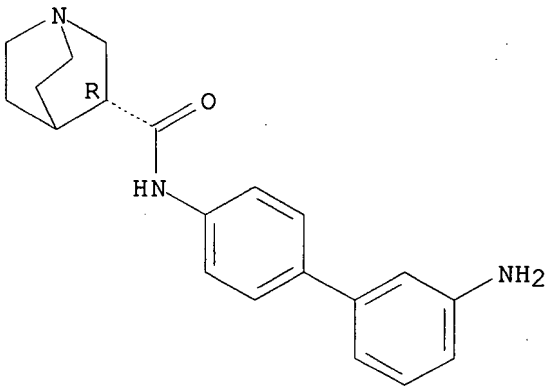
AB The invention relates to N-biarylamides I [R1 = NR2CONR3R4,NR2COCO2R5, NHSO2R6,SO2NHR7, NHCOR8; R2 = H, C1-6-alkyl; R3, R4 = H, C1-6-alkyl, C3-8-cycloalkyl, Ph (optionally substituted with up to three residues from the group halogen, CN, C1-6-alkyl, C1-6-alkoxy, CF3, OCF3); NR3R4 = 5- or 6-membered ring; R5 = H, C1-6-alkyl, C3-8-cycloalkyl, aryl, aryl-(C1-6-alkyl), R6 = C1-6-alkyl, C3-8-cycloalkyl, 5- or 6-membered heterocycle or heteroaryl, aryl-(C1-6-alkyl); R7 = C1-6-alkyl, C3-8-cycloalkyl, aryl, 5- or 6-membered heterocycle or heteroaryl, aryl-(C1-6-alkyl); R8 = C1-6-alkyl, C3-8-cycloalkyl, Ph, Ph-(C1-6-alkyl), (C1-6-alkoxy)-(C1-6-alkyl), (optionally substituted with up to three residues from the group halogen, CN, C1-6-alkyl, C1-6-alkoxy, CF3, OCF3)], their salts, solvates and salt solvates, methods for their production and use thereof for the production of medicaments for the treatment and/or prophylaxis of diseases and for improvement in cognition, concentration power, learning power and/or memory. Procedure for the preparation of I comprises: amidation of quinuclidine II [X = OH, Cl, OC6F5] with amines III or IV [Y = triflate, halogen (especially Br or I)]; with the latter, intermediate V is formed and is coupled with boronic acid VI [R9 = H, Me; (R9)2 = CH2CH2, CMe2CMe2] in an inert solvent containing a catalyst and a base. Thus, I·HCl [R1 = NHSO2Me-4] was prepared from quinuclidin-3-one via deoxidative cyanation, chromatog. resolution, hydrolysis, carbonyl chlorination and amidation with 4-(4-H2NC6H4)C6H4NHSO2Me. The binding ability of I·HCl [R1 = NHSO2Me-4] towards 7α-n acetylcholine receptor was determined [Ki = 2 nM].

IT 838852-86-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation, sulfonation or carbamylation of; preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)

RN 838852-86-1 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(3'-amino[1,1'-biphenyl]-4-yl)-, dihydrochloride, (3R)- (9CI) (CA INDEX NAME)

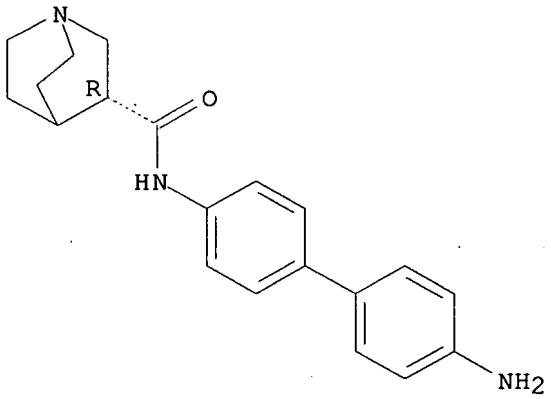
Absolute stereochemistry.



●2 HCl

IT 838852-85-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation, sulfonylation or carbamylation of; preparation of
quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)
RN 838852-85-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-amino[1,1'-biphenyl]-4-yl)-, dihydrochloride, (3R)- (9CI) (CA INDEX NAME)

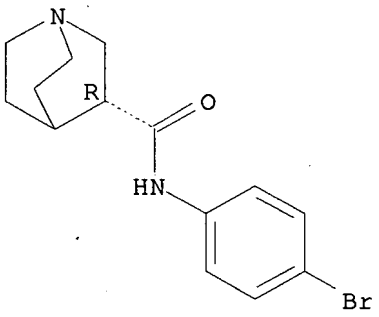
Absolute stereochemistry.



●2 HCl

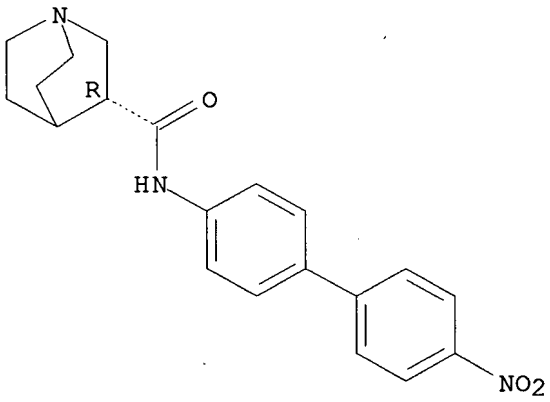
IT 604803-85-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and coupling reactions of, with boronates; preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)
RN 604803-85-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 838852-84-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of; preparation of quinuclidine N-biarylamides
for use in treatment and/or prophylaxis of diseases)
RN 838852-84-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-nitro[1,1'-biphenyl]-4-yl)-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

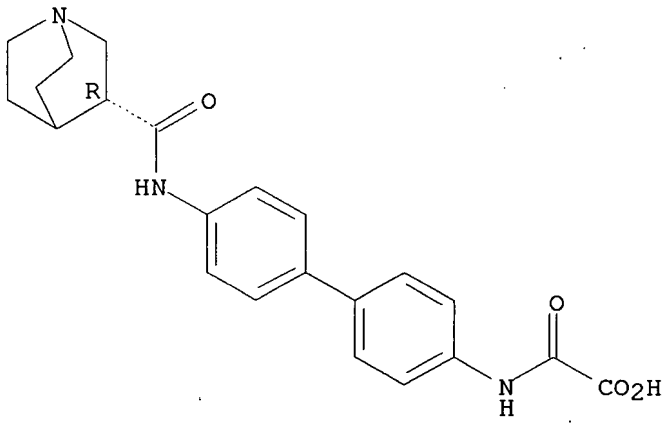
Absolute stereochemistry.



● HCl

IT 838852-67-8P 838852-68-9P 838852-69-0P
838852-70-3P 838852-71-4P 838852-72-5P
838852-73-6P 838852-74-7P 838852-75-8P
838852-76-9P 838852-77-0P 838852-78-1P
838852-79-2P 838852-80-5P 838852-81-6P
838852-82-7P 838852-83-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinuclidine N-biarylamides for use in treatment and/or prophylaxis of diseases)
RN 838852-67-8 CAPLUS
CN Acetic acid, [[4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino][1,1'-biphenyl]-4-yl]amino]oxo-, monohydrochloride (9CI) (CA INDEX NAME)

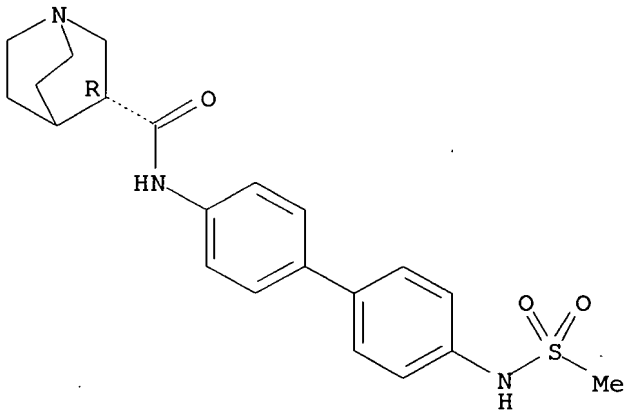
Absolute stereochemistry.



● HCl

RN 838852-68-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(methylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)-(9CI) (CA INDEX NAME)

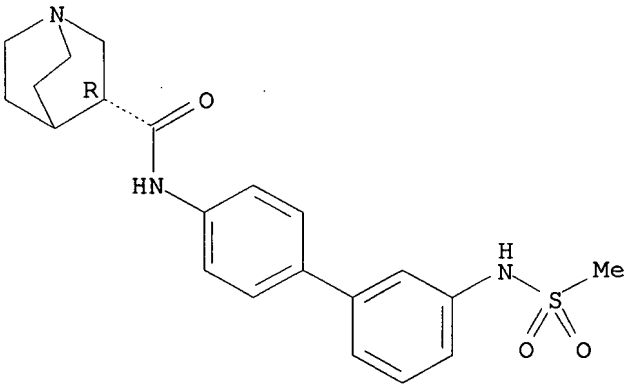
Absolute stereochemistry.



● HCl

RN 838852-69-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[3'-[(methylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)-(9CI) (CA INDEX NAME)

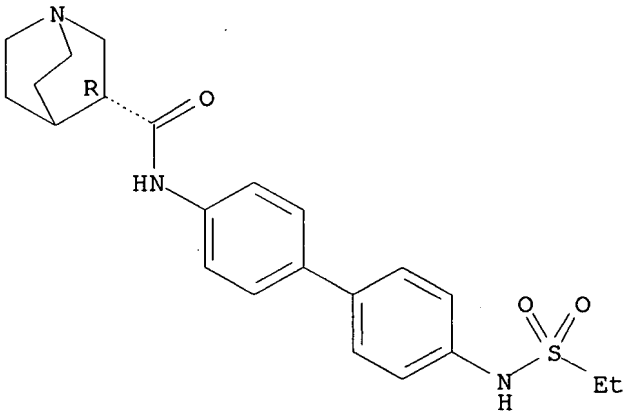
Absolute stereochemistry.



● HCl

RN 838852-70-3 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(ethylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

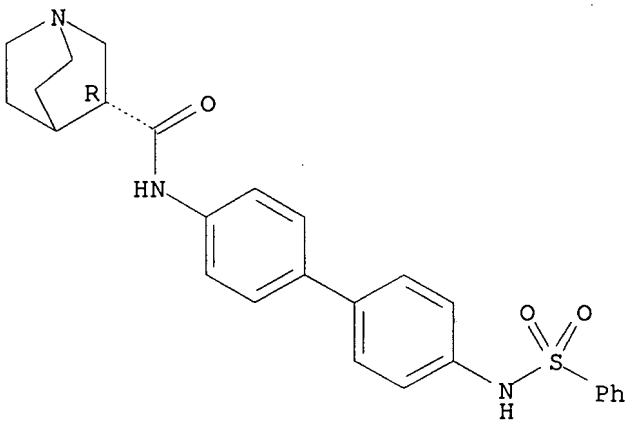
Absolute stereochemistry.



● HCl

RN 838852-71-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(phenylsulfonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

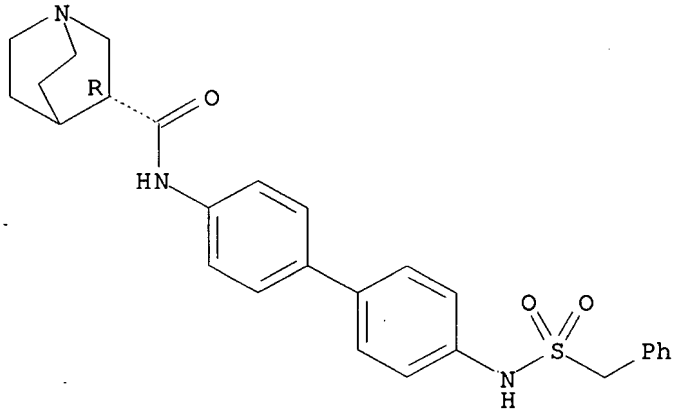
Absolute stereochemistry.



● HCl

RN 838852-72-5 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(phenylmethyl)sulfonyl]amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

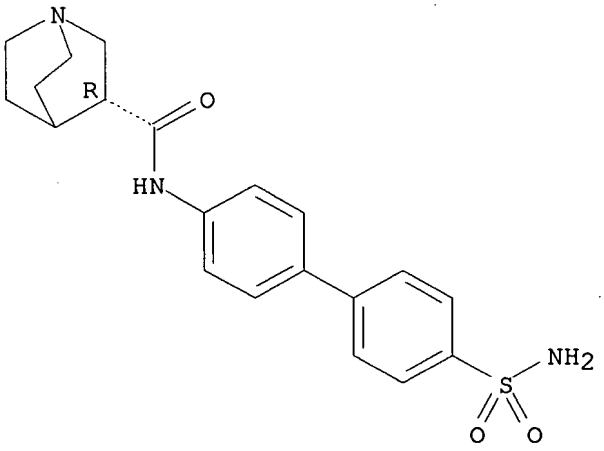
Absolute stereochemistry.



● HCl

RN 838852-73-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

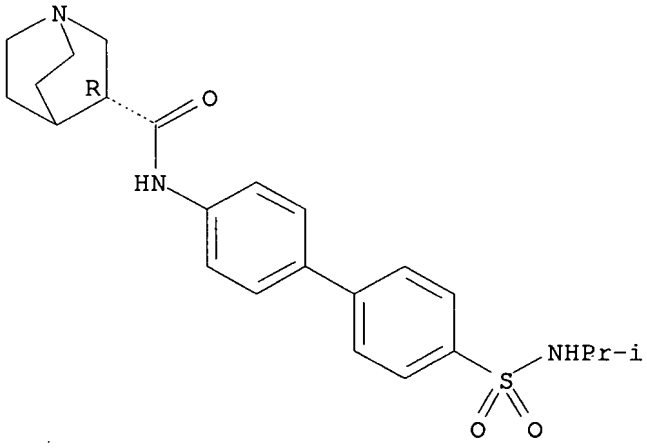
Absolute stereochemistry.



● HCl

RN 838852-74-7 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(1-methylethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

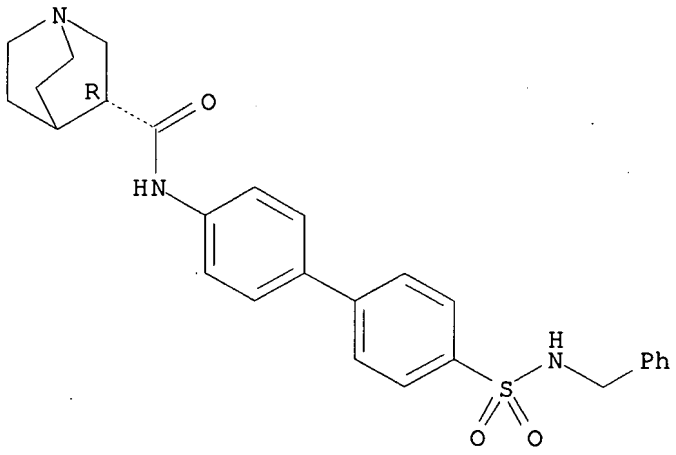
Absolute stereochemistry.



● HCl

RN 838852-75-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(phenylmethyl)amino]sulfonyl][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

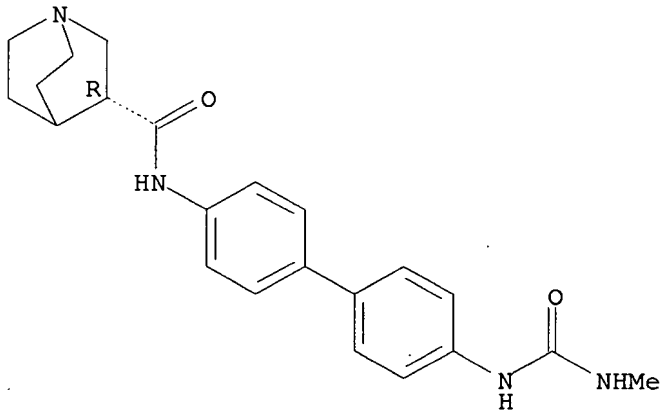
Absolute stereochemistry.



● HCl

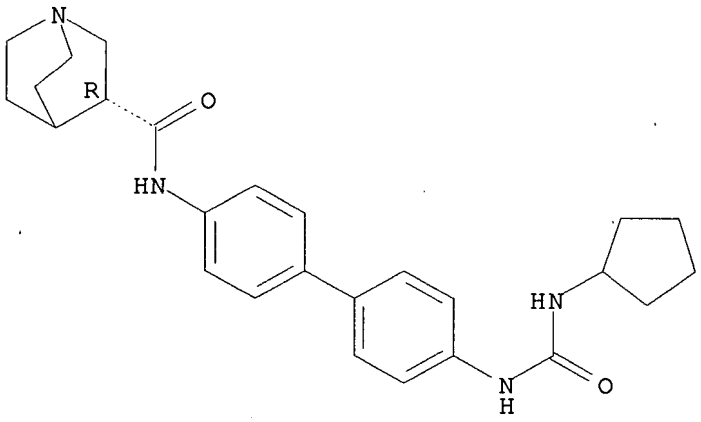
RN 838852-76-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(methylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 838852-77-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(cyclopentylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

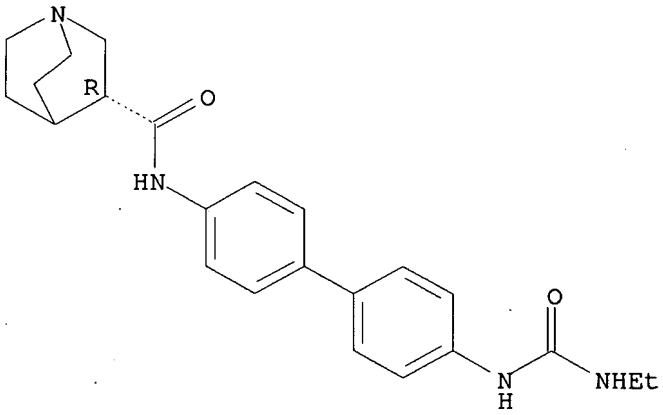
Absolute stereochemistry.



● HCl

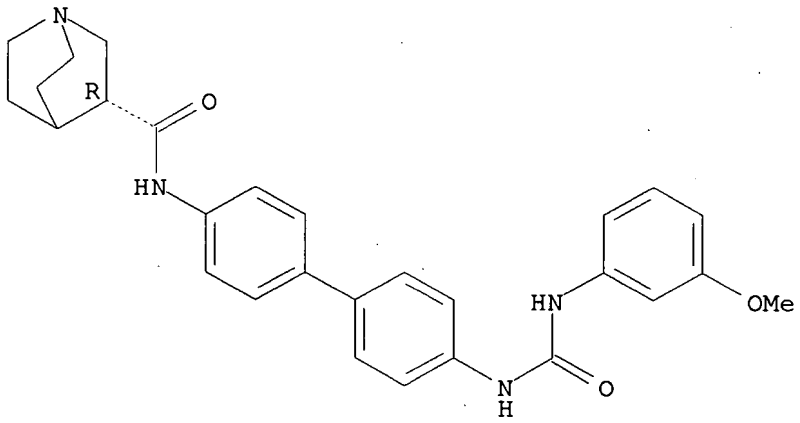
RN 838852-78-1 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[(ethylamino)carbonyl]amino][1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 838852-79-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[[(3-methoxyphenyl)amino]carbonyl]amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

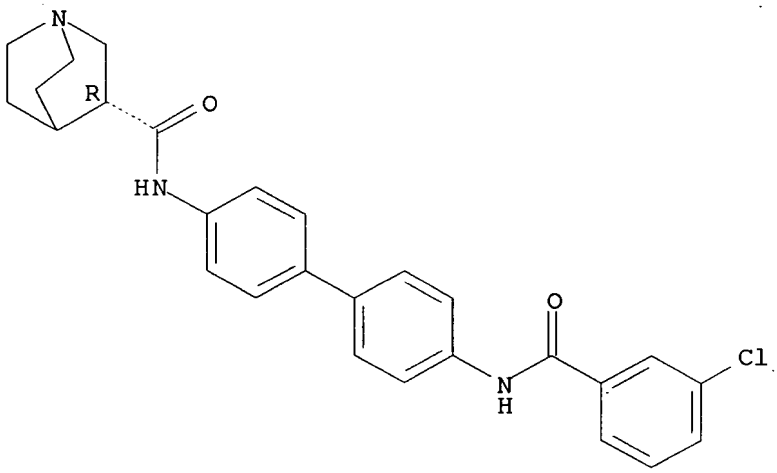
Absolute stereochemistry.



● HCl

RN 838852-80-5 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(3-chlorobenzoyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

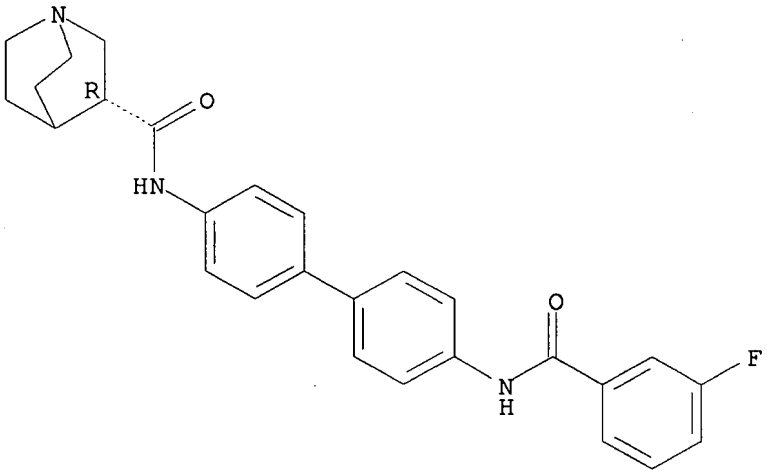
Absolute stereochemistry.



● HCl

RN 838852-81-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(3-fluorobenzoyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

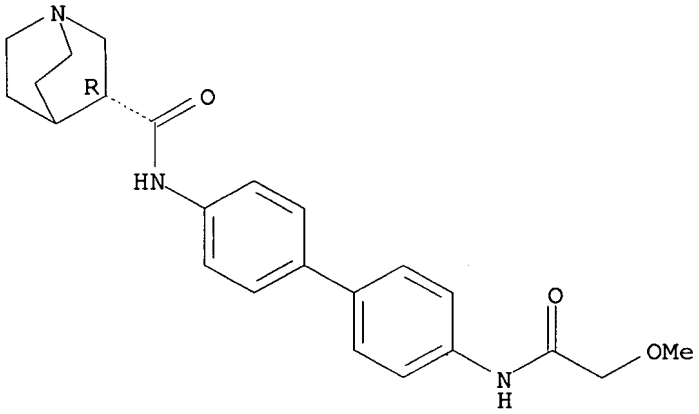
Absolute stereochemistry.



● HCl

RN 838852-82-7 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(methoxyacetyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

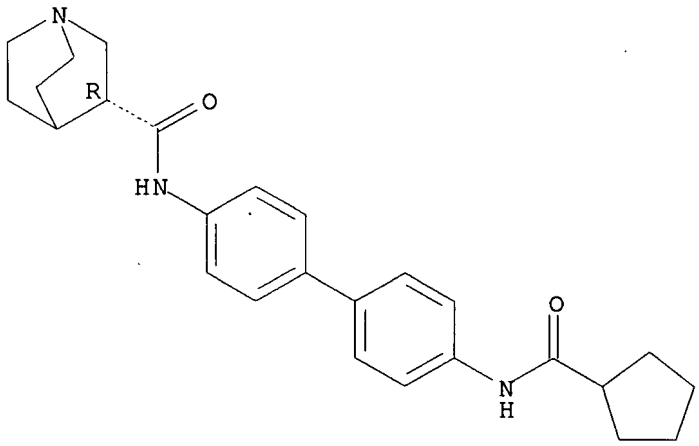
Absolute stereochemistry.



● HCl

RN 838852-83-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[(cyclopentylcarbonyl)amino][1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:757707 CAPLUS
DOCUMENT NUMBER: 139:277050
TITLE: Preparation of aza-bicyclic N-biarylamides with affinity for the α7-nicotinic acetylcholine receptor
INVENTOR(S): Luithle, Joachim; Boess, Frank-Gerhard; Erb, Christina; Schnizler, Katrin; Flessner, Timo; Van Kampen, Marja; Methfessel, Christoph; Hafner, Frank-Thorsten
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

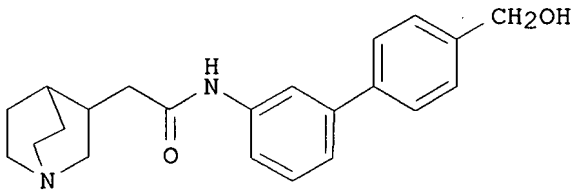
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078431	A1	20030925	WO 2003-EP2153	20030303
WO 2003078431	A8	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10211415	A1	20030925	DE 2002-10211415	20020315
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
AU 2003212296	A1	20030929	AU 2003-212296	20030303
EP 1487834	A1	20041222	EP 2003-708168	20030303
EP 1487834	B1	20070425		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2005154045	A1	20050714	US 2003-508108		20030303
US 7138410	B2	20061121			
JP 2005524675	T	20050818	JP 2003-576436		20030303
PRIORITY APPLN. INFO.:			DE 2002-10211415	A	20020315
			WO 2003-EP2153	W	20030303

OTHER SOURCE(S): MARPAT 139:277050

GI



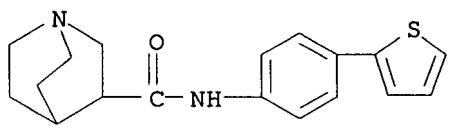
I

AB The azabicyclic N-arylamides, R1AC(:O)NR3ER3 [R1 = 1-azabicyclo[m.n.p]alkyl (7 - 11 ring atoms, optionally substituted with C1-6-alkyl); m, n = 2, 3; p = 1, 2, 3; A = CH2, CH2CH2, propylene; E = 5-6 membered heteroaryl of benzenediyl optionally substituted with halo, cyano, F3C, F3CO, C1-6-alkyl; R2 = 5-6 membered heteroaryl, Ph, optionally substituted with halo, heterocyclyl, carbamoyl, carboxylate, amino, acyl, CN, CF3, CF3O, NO2, C1-6-alkyl, C1-6-alkoxy, C1-6-alkylthio, etc.; R3 = H, C1-6-alkyl] and their salts, solvates and salt solvates were prepared and used for producing pharmaceuticals for the treatment and/or prophylaxis of diseases and for improving perception, concentration, learning ability and memory. Thus, 2-(1-azabicyclo[2.2.2]octan-3-yl)-N-(3-bromophenyl)acetamide hydrochloride was treated with 4-(hydroxymethyl)phenylboronic acid to give the quinuclidineacetamide derivative I. The affinity of I for α7-nAChR was determined

IT 604803-22-7P 604803-23-8P 604803-24-9P
604803-25-0P 604803-34-1P 604803-35-2P
604803-36-3P 604803-37-4P 604803-38-5P
604803-39-6P 604803-40-9P 604803-41-0P
604803-42-1P 604803-44-3P 604803-45-4P
604803-47-6P 604803-49-8P 604803-97-6P
604804-00-4P 604804-02-6P 604804-04-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aza-bicyclic N-biarylamides with affinity for α-7 nicotinic acetylcholine receptor)

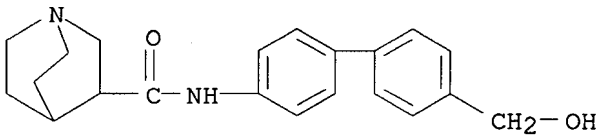
RN 604803-22-7 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4-(2-thienyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



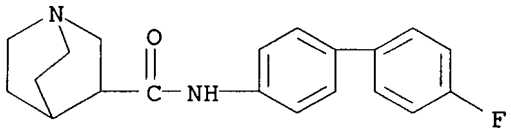
● HCl

RN 604803-23-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



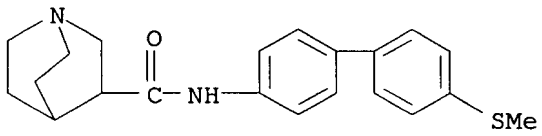
● HCl

RN 604803-24-9 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-fluoro[1,1'-biphenyl]-4-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

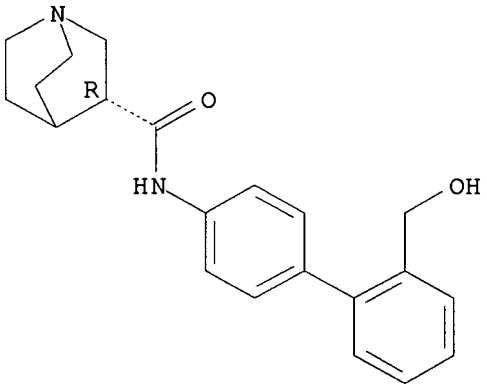
RN 604803-25-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(methylthio)[1,1'-biphenyl]-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

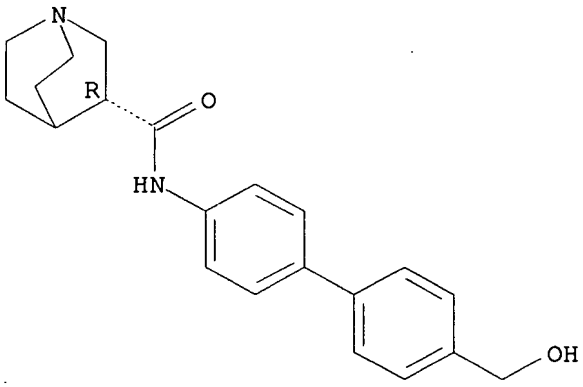
RN 604803-34-1 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[2'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 604803-35-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

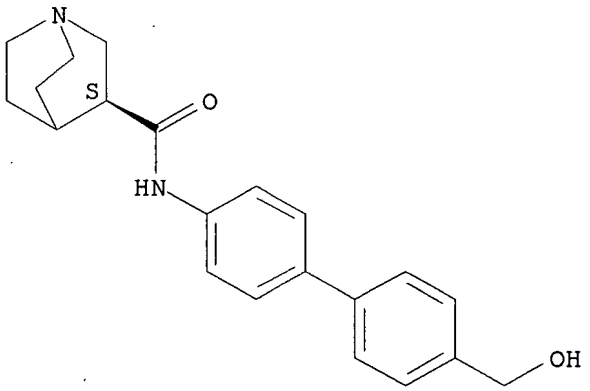
Absolute stereochemistry.



● HCl

RN 604803-36-3 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

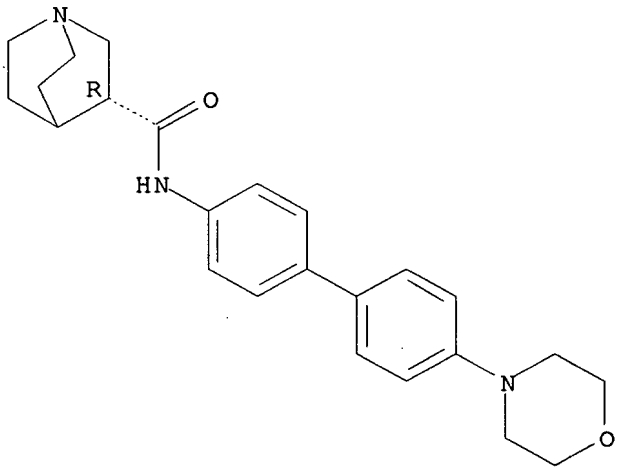
Absolute stereochemistry.



● HCl

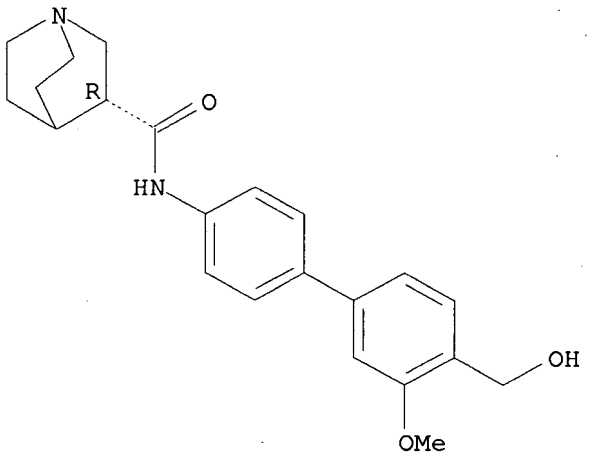
RN 604803-37-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(4-morpholinyl)[1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



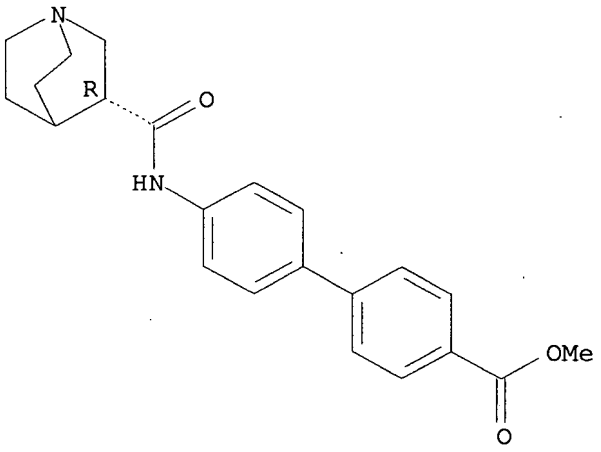
RN 604803-38-5 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)-3'-methoxy[1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



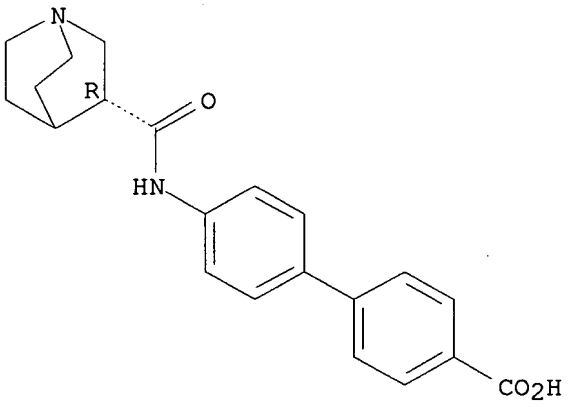
RN 604803-39-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 604803-40-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

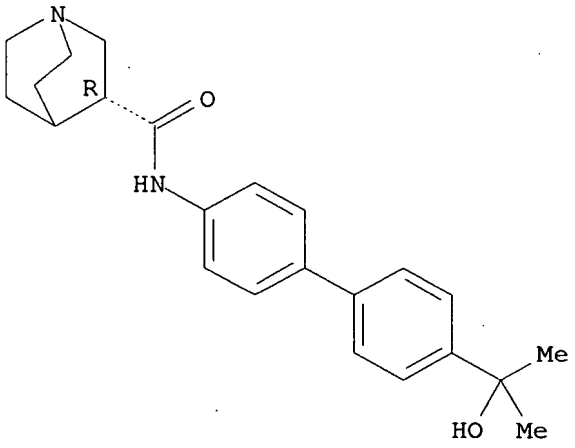
Absolute stereochemistry.



● HCl

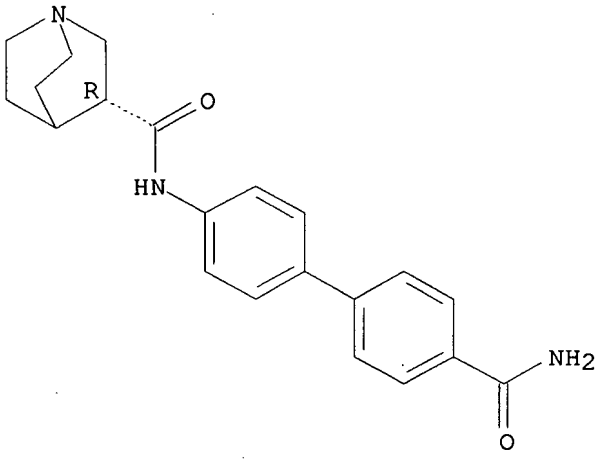
RN 604803-41-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(1-hydroxy-1-methylethyl)[1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 604803-42-1 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(aminocarbonyl)[1,1'-biphenyl]-4-yl]-, hydrochloride, (3R)- (9CI) (CA INDEX NAME)

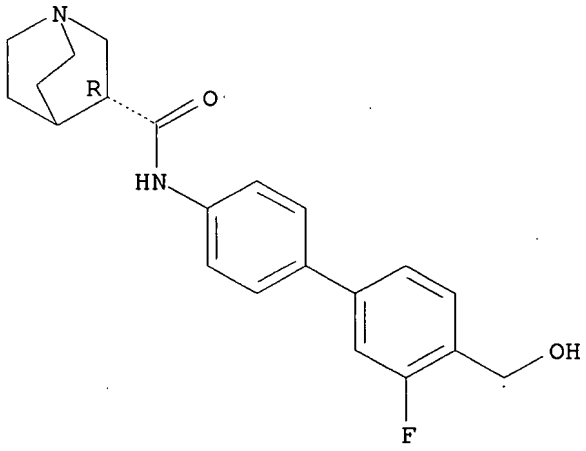
Absolute stereochemistry.



● x HCl

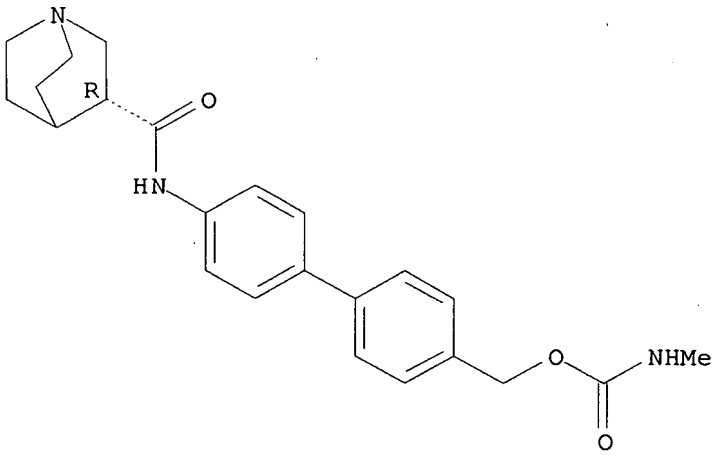
RN 604803-44-3 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[3'-fluoro-4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



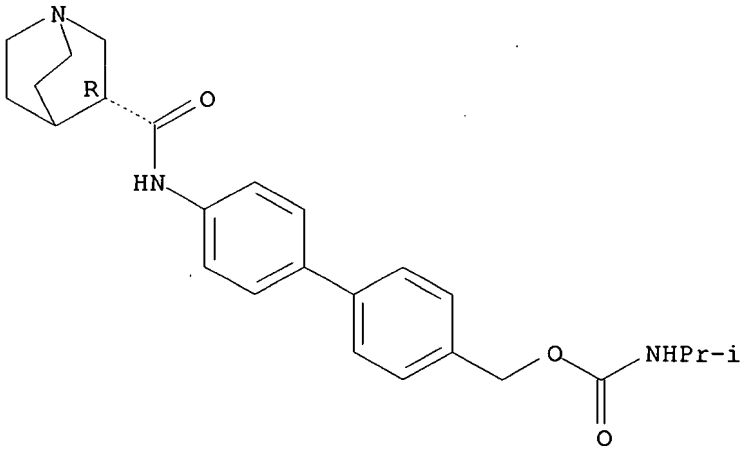
RN 604803-45-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-[[[(methylamino)carbonyl]oxy]methyl][1,1'-biphenyl]-4-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



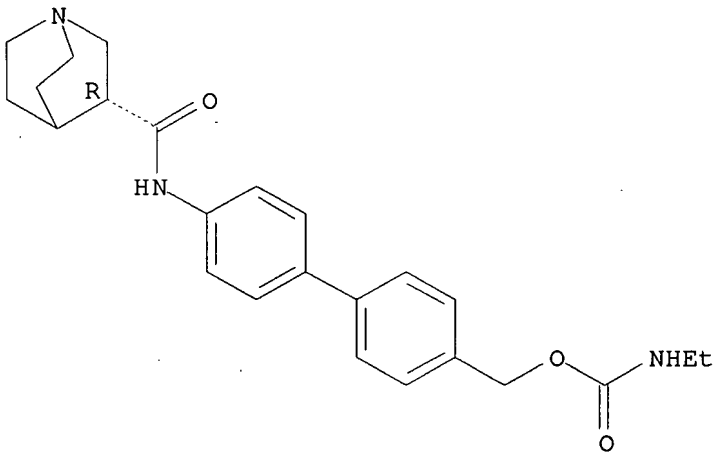
RN 604803-47-6 CAPLUS
CN Carbamic acid, (1-methylethyl)-, [4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino][1,1'-biphenyl]-4-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

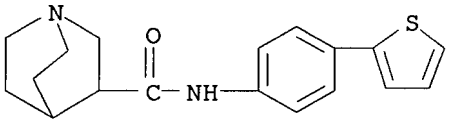


RN 604803-49-8 CAPLUS
CN Carbamic acid, ethyl-, [4'-[[(3R)-1-azabicyclo[2.2.2]oct-3-ylcarbonyl]amino][1,1'-biphenyl]-4-yl]methyl ester (9CI) (CA INDEX NAME)

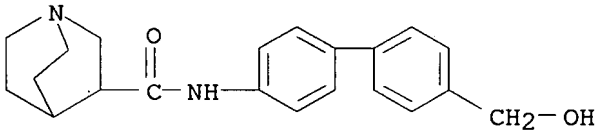
Absolute stereochemistry.



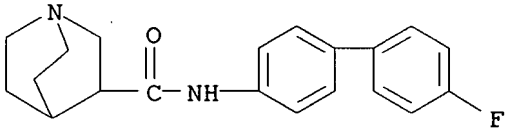
RN 604803-97-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4-(2-thienyl)phenyl]- (9CI) (CA INDEX NAME)



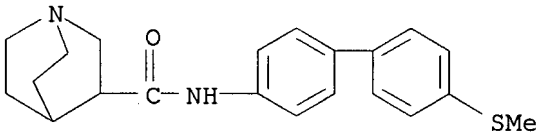
RN 604804-00-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)



RN 604804-02-6 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4'-fluoro[1,1'-biphenyl]-4-yl)- (9CI) (CA INDEX NAME)

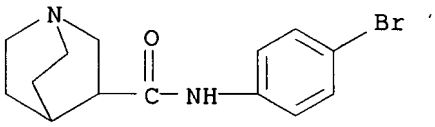


RN 604804-04-8 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4'-(methylthio)[1,1'-biphenyl]-4-yl]- (9CI) (CA INDEX NAME)



IT 604803-72-7P 604803-83-0P 604803-85-2P
604804-18-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aza-bicyclic N-biarylamides with affinity for α-7 nicotinic acetylcholine receptor)

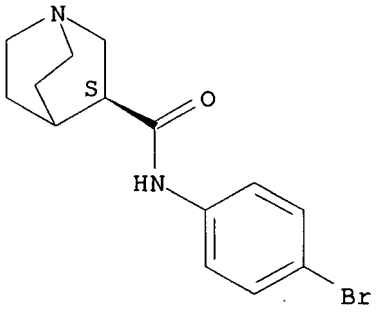
RN 604803-72-7 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

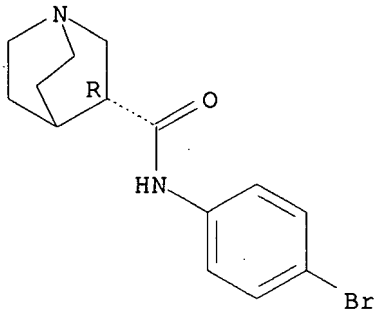
RN 604803-83-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

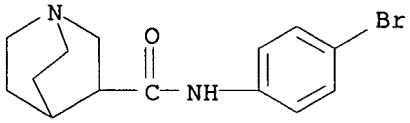


RN 604803-85-2 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 604804-18-4 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(4-bromophenyl)- (9CI) (CA INDEX NAME)

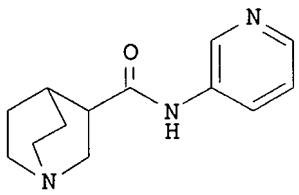


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:506550 CAPLUS
DOCUMENT NUMBER: 139:85529
TITLE: Preparation of monocyclic N-aryl amides for improvement of the perception and memory enhancement
INVENTOR(S): Luithle, Joachim; Boess, Frank-Gerhard; Erb, Christina; Flessner, Timo; Hendrix, Martin; Van Kampen, Marja; Methfessel, Christoph
PATENT ASSIGNEE(S): Bayer AG, Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10162442	A1	20030703	DE 2001-10162442	20011219
PRIORITY APPLN. INFO.:			DE 2001-10162442	20011219

OTHER SOURCE(S): MARPAT 139:85529
GI

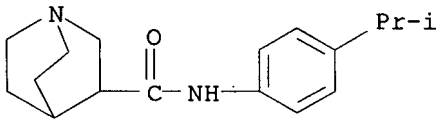


AB The invention concerns the use of monocyclic N-aryl amides, R1CONR2R3 [R1 = 1-azabicyclo[m.n.p]alkyl (7 - 11 ring atoms, optionally substituted with C1-6-alkyl); m, n = 2 , 3; p = 1 - 3; R2 = (un)substituted Ph, 5 to 6-membered heteroaryl (optionally substituted with halogen, CHO, CONH2, CN, CF3,CF3O, NO2, C1-6-alkyl, C1-6-alkoxy, C1-6-alkylthio); R3 = H, C1-6-alkyl] and their salts, solvates and solvate salts, in the production of drugs for the improvement of the perception, concentration achievement, learning achievement and/or memory achievement as well as to new monocyclic N-aryl amides. Thus, N-(3-pyridinyl)quinuclidine-3-carboxamide dihydrochloride(I·2HCl) was prepared from quinuclidine-3-carboxylic acid chloride hydrochloride and 3-aminopyridine in DMF containing EtN(CHMe2)2 and catalytic DMAP. The affinity of I for α7-nAChR was determined (no data).

IT 552832-93-6P, N-(4-Isopropylphenyl)quinuclidine-3-carboxamide hydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of monocyclic N-aryl amides for improvement of the perception and memory enhancement)

RN 552832-93-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-[4-(1-methylethyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:199358 CAPLUS

DOCUMENT NUMBER: 114:199358

TITLE: EO-199, a specific antagonist of antiarrhythmic drugs: assessment by binding experiments and in vivo studies

AUTHOR(S): Oppenheimer, Edna; Harel, Gideon; Lipinsky, Dafna; Sarne, Yosef

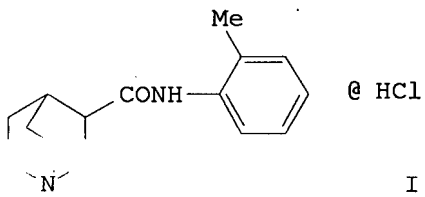
CORPORATE SOURCE: Sackler Fac. Med., Tel-Aviv Univ., Ramat-Aviv, 69978, Israel

SOURCE: Life Sciences (1991), 48(10), 977-85
CODEN: LIFSAK; ISSN: 0024-3205

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



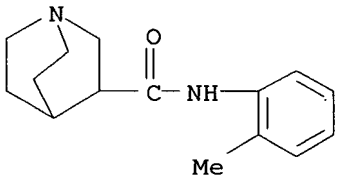
I

AB EO-199 (I), a demethylated analog of the novel class I antiarrhythmic drug EO-122, was found to antagonize the antiarrhythmic activity of EO-122 and that of procainamide (Class I). EO-199 did not block the activity of a class IB antiarrhythmic agent, lidocaine. EO-199 also displaced the specific binding of [3H]EO-122 to rat heart membranes similarly to procainamide, whereas lidocaine did not. The correlation between binding expts. and pharmacol. effects points to a possible subclassification of these drugs. The 2 chemical analogs EO-199 and EO-122, as well as procainamide (IA) but not lidocaine (IB), compete at the same site or the same state of the sodium channel. The availability of a specific antagonist might be useful for studying the mechanism of action of antiarrhythmic drugs as well as an antidote in cases of antiarrhythmics overdose intoxication.

IT 133658-30-7, EO 199
RL: BIOL (Biological study)
(antiarrhythmic agents antagonism by, poisoning by antiarrhythmics in relation to)

RN 133658-30-7 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2-methylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:69427 CAPLUS

DOCUMENT NUMBER: 112:69427

TITLE: Molecular modeling studies on class Ia and Ib antiarrhythmics. Model representations for differentiating binding sites

AUTHOR(S): Marrer, S.

CORPORATE SOURCE: Pharm. Inst., Freie Univ. Berlin, Berlin, Fed. Rep. Ger.

SOURCE: Pharmaceutica Acta Helvetiae (1989), 64(12), 338-44
CODEN: PAHEAA; ISSN: 0031-6865

DOCUMENT TYPE: Journal

LANGUAGE: German

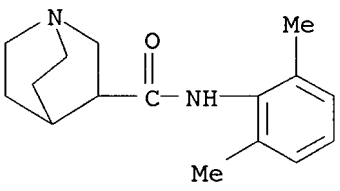
AB The mol. properties of quinidine, EO 122, and lidocaine were investigated using theor. mol. modeling. The binding patterns of the mols. were investigated by calculating interaction energies with a neg. charged fragment (receptor model). Based on these calcns. a model for the differentiation of class Ia and class Ib antiarrhythmic drugs could be deduced. The results fit the modulated receptor hypothesis. The mol. basis for the preferred affinity of quinidine to the open state of the sodium channel and the equal affinity of lidocaine to the open and inactivated state of the channel were defined.

IT 23581-62-6, EO-122
RL: BIOL (Biological study)
(mol. modeling of heart sodium channel receptor interaction with)

RN 23581-6-6 CAPLUS

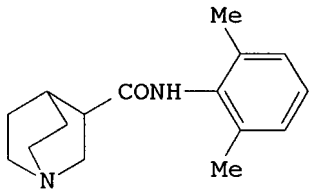
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-,

monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:400428 CAPLUS
DOCUMENT NUMBER: 111:428
TITLE: The specific binding of [3H]EO-122, a radiolabeled class I antiarrhythmic drug, to rat heart membranes
AUTHOR(S): Oppenheimer, Edna; Meiri, Hamutal; Ori, Yaacov
CORPORATE SOURCE: Sackler Fac. Med., Tel Aviv Univ., Ramat Aviv, 69978, Israel
SOURCE: Journal of Molecular and Cellular Cardiology (1989), 21(2), 223-30
CODEN: JMCDAY; ISSN: 0022-2828
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



@ HCl

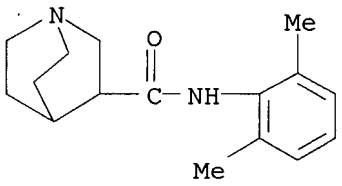
I

AB [3H]EO-122 (I), a radiolabeled class I antiarrhythmic drug, was used to characterize a new specific binding system to rat heart membranes. The binding was saturable and competitive with unlabeled EO-122 and other antiarrhythmic drugs. In this system, [3H]EO-122 bound to 2 sites: site A with an apparent Kd of 33.5 nM, Bmax of 1.05 pmol/mg protein and Hill coefficient nH = 4 and site B with an apparent Kd of 233 nM, Bmax of 5.7 pmol/mg protein and nH = 6. The binding to site B indicates that this site is pharmacol. relevant to known class IA antiarrhythmic drugs such as quinidine and procainamide. Lidocaine (class IB) did not interact with this site. Interpretation of the high Hill coefficient suggests that the binding of an antiarrhythmic drug to its pharmacol. relevant binding site exposes addnl. binding sites and/or modulates the affinity of adjacent binding sites.

IT 23581-62-6, EO 122
RL: PROC (Process)
(binding of, by heart membrane)

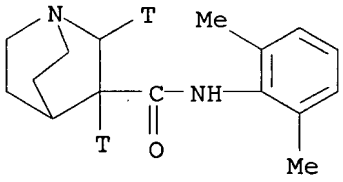
RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



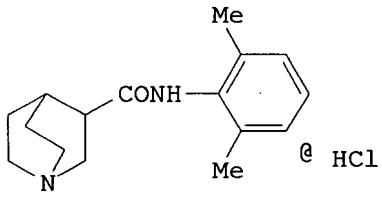
● HCl

IT 120949-68-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and binding by heart membrane of)
RN 120949-68-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-2,3-t2-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:611641 CAPLUS
DOCUMENT NUMBER: 107:211641
TITLE: Electrophysiological effects of a novel antiarrhythmic drug, EO-122, on guinea pig ventricular muscle and isolated myocytes
AUTHOR(S): Binah, Ofer; Gilat, Eran; Rubinstein, Irit; Oppenheimer, Edna
CORPORATE SOURCE: Rappaport Family Inst. Res. Med. Sci., Fac. Med., Haifa, 31096, Israel
SOURCE: Journal of Cardiovascular Pharmacology (1987), 10(3), 301-8
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

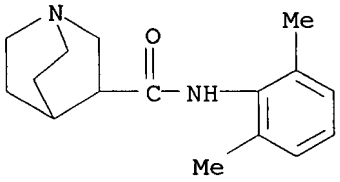
AB The effects of EO-122 (I) on the electrophysiol. properties of guinea pig papillary muscle and ventricular myocytes were investigated by means of

standard microelectrode and whole-cell recording techniques, resp. At the concentration range of 10-7-10-4 M (cycle length, 2000 ms), resting potential and action potential duration (APD90) were not altered by the drug. Action potential amplitude and APD50 were reduced by 10-4 M, and Vmax was reduced by EO-122 ≥10-5 M. The effect of EO-122 on Vmax was use-dependent. At 10-6 and 10-5 M (cycle length, 2000 ms), the time constant for onset of block (τon) was 37.0 and 26.0 s, resp. The recovery kinetics from use-dependent block was not monoexponential, and the estimated "time constant" for recovery was 76.5 s. The effects of EO-122, 10-5 M on the membrane currents in ventricular myocytes were examined and it was found that the drug attenuated the slow inward current (Isi). The present study demonstrates that EO-122 blocks both the fast inward (Na+) and the slow inward (Ca2+) channels, and these effects are probably responsible for the antiarrhythmic effects of the drug.

IT 23581-62-6, EO-122
RL: BIOL (Biological study)
(heart elec. activity response to, antiarrhythmic mechanism in relation to)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1981:424851 CAPLUS
DOCUMENT NUMBER: 95:24851
TITLE: Process for the preparation of quinuclidine carboxylic acid derivatives
PATENT ASSIGNEE(S): Mundipharma A.-G., Switz.
SOURCE: Brit., 3 pp. Division of Brit. 1,578,421.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1578422	A	19801105	GB 1979-21014	19780119
IL 51296	A	19831031	IL 1977-51296	19770119
GB 1578421	A	19801105	GB 1978-2197	19780119
PRIORITY APPLN. INFO.:			IL 1977-51296 A	19770119
			GB 1978-2197	19780119

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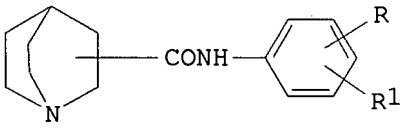
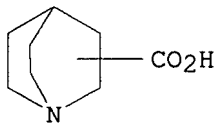
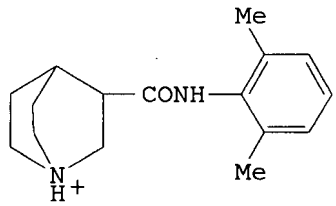


I



II



Cl^-

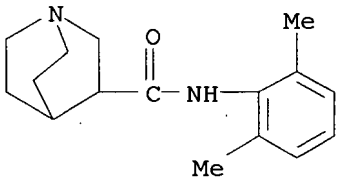
III

AB The title compds. I (R, R1 = H, halo, C1-6 alkyl) were prepared by treating a quinuclidinecarboxylate II or its acid addition salts with H2NC6H3RR1 (R, R1 as before) in anhydrous alc.-free CHCl3 containing (COCl)2. E.g., 2.5 g of the HCl addition salt of II (CO2H group in 3-position) was refluxed 3 h in 150 mL anhydrous alc.-free CHCl3 containing 10 mL (COCl)2, then treated with 3 g H2NC6H3Me2-2,6 in 100 mL CHCl3 (reflux, 6 h) to give, after work-up, 3 g (91%) III. III has useful antiarrhythmic properties (no data).

IT 23581-62-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, of, as antiarrhythmic)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:561251 CAPLUS

DOCUMENT NUMBER: 93:161251

TITLE: A preclinical study of EO-122, a new lidocaine-like antiarrhythmic drug

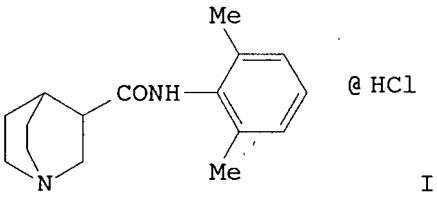
AUTHOR(S): Oppenheimer, Edna; Kaplinsky, Eliezer; Kariv, Naam; Bruckstein, Rachel; Cohen, Sasson

CORPORATE SOURCE: Sackler Sch. Med., Tel-Aviv Univ., Kfar Saba, Israel

SOURCE: Angiology (1980), 31(6), 410-26
CODEN: ANGIAB; ISSN: 0003-3197

DOCUMENT TYPE: Journal

LANGUAGE: English



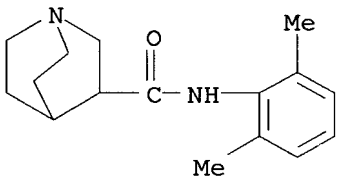
I

AB Restoration of normal sinus rhythm and suppression of ouabain-induced arrhythmia in cats and dogs, and of coronary occlusion-induced arrhythmia in dogs, followed a single i.v. injection of 1-3 mg EO 122 (I) [23581-62-6]/kg, with an onset of 2 min and a duration of 20-240 min. Occlusion-induced arrhythmia was also suppressed after an oral dose of 10-20 mg/kg, with an onset of 11-65 min and a duration of 25-120 min. Under similar conditions, lidocaine was either totally ineffective or of ultra-short duration. The bioavailability of EO-122 by the oral route exceeded 80% of the oral dose. Therapeutic blood concns. were in the range 0.5-7 μg/mL. At about 5 μg/mL, there was a slight depression of cardiac function in the anesthetized cat, but not in the conscious dog. In cats, complete A-V block occurred at concns. of 60-70 μg/mL. The i.v. LD50 in mice was 22 mg/kg and in rabbits 8.5 mg/kg. No overt signs of neurotoxicity could be observed at any dose of EO-122. The pharmacokinetic profile of the drug fits a two-compartment open model, with t1/2 .simeq.150 min.

IT 23581-62-6
RL: BIOL (Biological study)
(heart arrhythmia response to)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1979:92467 CAPLUS

DOCUMENT NUMBER: 90:92467

TITLE: Solvent-caused quaternization as a possible source of error in the mass spectral quantitation of tertiary amines. I. Methylene chloride quaternization

AUTHOR(S): Vincze, Adam; Gefen, Leon

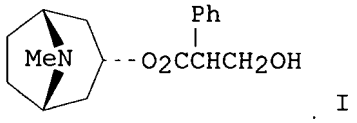
CORPORATE SOURCE: Israel Inst. Biol. Res., Ness Ziona, Israel

SOURCE: Israel Journal of Chemistry (1978), 17(3), 236-8
CODEN: ISJCAT; ISSN: 0021-2148

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



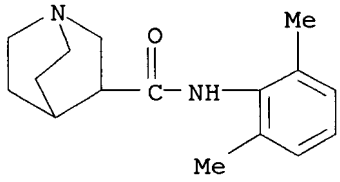
I

AB Basic tertiary amines such as atropine (I) [51-55-8] and derivs. of N-methylpiperidine and quinuclidine, tend to quaternize in CH2Cl2 [75-09-2] at room temperature The quaternary ammonium salts formed undergo various dequaternization reactions in the heated direct inlet probe of the mass spectrometer, giving rise to volatile tertiary amines that are different from the starting material and usually having higher mol. wts. Recorded spectra of such samples are a superposition of those of the various tertiary amines constituting the mixture If just a few relevant and abundant ions in the mass spectrum of the original tertiary amine are monitored, as in quant. fragmentog. rather low results might be obtained. Moreover, the operator may be quite unaware of the fact that only part of the sample is being measured.

IT 69267-68-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylene chloride quaternization of, mass spectroscopic error in relation to)

RN 69267-68-1 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)- (9CI) (CA INDEX NAME)



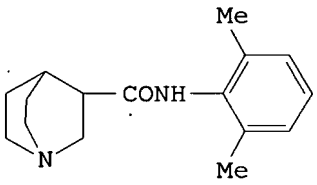
L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1978:546786 CAPLUS
DOCUMENT NUMBER: 89:146786
TITLE: Antiarrhythmic quinuclidine carboxylic acid xylidide
INVENTOR(S): Oppenheimer, Edna; Kaplinsky, Eliezer; Cohen, Sasson
PATENT ASSIGNEE(S): Mundipharma A.-G., Switz.
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2802208	A1	19780720	DE 1978-2802208	19780119
IL 51296	A	19831031	IL 1977-51296	19770119
ZA 7707476	A	19781025	ZA 1977-7476	19771215
FI 7703923	A	19780720	FI 1977-3923	19771223
ES 465827	A1	19790101	ES 1978-465827	19780107
SE 7800204	A	19780720	SE 1978-204	19780109
SE 443786	B	19860310		
[illegible]	[illegible]	[illegible]		
AU 7032469	A	19790726	AU 1978-32469	19780117
AU 519089	B2	19811105		
DK 7800264	A	19780720	DK 1978-264	19780118

DK 147180	B	19840507		
DK 147180	C	19841112		
NO 7800177	A	19780720	NO 1978-177	19780118
NO 148335	B	19830613		
NO 148335	C	19830921		
FR 2384499	A1	19781020	FR 1978-1354	19780118
FR 2384499	B1	19811030		
AT 7800353	A	19790815	AT 1978-353	19780118
AT 355586	B	19800310		
CA 1107734	A1	19810825	CA 1978-295163	19780118
JP 53109952	A	19780926	JP 1978-4764	19780119
JP 63008111	B	19880219		

PRIORITY APPLN. INFO.: IL 1977-51296 A 19770119
OTHER SOURCE(S): MARPAT 89:146786
GI



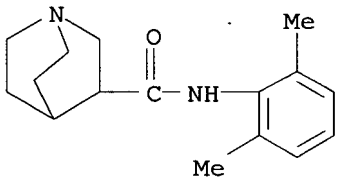
I

AB The title compound (I) was prepared in 91% yield by treating 3-quinuclidinecarboxylic acid-HCl with oxalyl chloride and 2,6-Me2C6H3NH2. I has superior antiarrhythmic activity to lidocaine. The 2-quinuclidine analog of I is inactive and neurotoxic.

IT 23581-62-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiarrhythmic activity of)

RN 23581-62-6 CAPLUS

CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



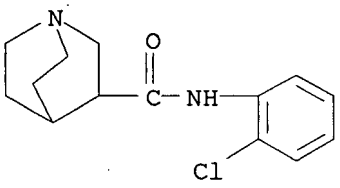
● HCl

L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:78905 CAPLUS
DOCUMENT NUMBER: 72:78905
TITLE: 2(and 3)-Quinuclidine carboxanilides
INVENTOR(S): Sandberg, Bengt E. V.; Sjöberg, Bernhard O. V.; Tegner, Claes F.
PATENT ASSIGNEE(S): Aktiebolag Astra
SOURCE: Fr., 7 pp.

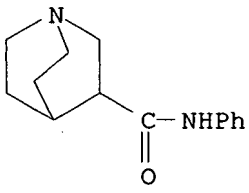
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1566045		19690502	FR	19680522
DE 1770414			DE	
FR 7713			FR	
GB 1176757			GB	
SE 331841			SE	
US 3579523		19710518	US	19680517
US 3726980		19730410	US	19701026

PRIORITY APPLN. INFO.: SE 19670523
OTHER SOURCE(S): MARPAT 72:78905
GI For diagram(s), see printed CA Issue.
AB The title compds. (I) and (II), which have antiarrhythmic and local anesthetic effects, were prepared from derivs. of quinuclidine-2(or 3)-carboxylic acids (Renk, E.; et al., 1954). Thus, a mixture of 4.5 g Me quinuclidine-2-carboxylate, 2.9 g o-toluidine, and 0.1 g Na was kept 5 hr at 140° and worked up to give 2.1 g I (R1 = H, R2 = Me), m. 115.5-17° (aqueous EtOH). Similarly prepared were the following I (R1, R2, and m.p. HCl salt given): H, Cl, - [base m. 117-19.5° (aqueous EtOH)]; Me, Me, 223-5° (EtOH-isoPr2O); Me, Et, 209-11° (MeCOPr); Et, Et, 209.5-11.5° (MeCN). Also prepared were II (R = Cl), m. 166.5-8.5° (MeCOBu-iso), and II (R = H), m. 178-80° (MeCOBu-iso).
IT 26801-43-4P 26801-44-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 26801-43-4 CAPLUS
CN 3-Quinuclidinecarboxanilide, 2'-chloro- (8CI) (CA INDEX NAME)



RN 26801-44-5 CAPLUS
CN 3-Quinuclidinecarboxanilide (8CI) (CA INDEX NAME)



L4 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1969:461176 CAPLUS
DOCUMENT NUMBER: 71:61176
TITLE: Some derivatives of quinuclidine-3-carboxylic acids
AUTHOR(S): Dahlbom, Richard; Dolby, Jorgen

CORPORATE SOURCE: Farm. Fak. Stockholm, Stockholm, Swed.
SOURCE: Acta Pharmaceutica Suecica (1969), 6(2), 277-82
CODEN: APSXAS; ISSN: 0001-6675
DOCUMENT TYPE: Journal
LANGUAGE: English

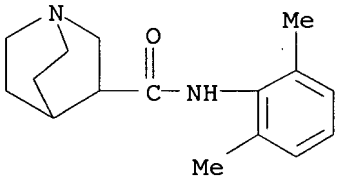
GI For diagram(s), see printed CA Issue.

AB Me dehydroquinuclidine-3-carboxylate-HCl (Ia.HCl) (2.4 g.) in 20 ml. 33% aqueous MeNH2 was kept 48 hrs. at room temperature, and worked up to give 54% I (R = NHMe), m. 201-2°. Other amides similarly prepared were as follows [compound type, R (or R and R1), % yield, salt, and m.p. salt given]: II, NHMe, H, 47, HCl, 229-30°; II, NHEt, H, 40, HCl, 270-1°; I, NHEt, 63, oxalate, 169-72°; I, NHPr, 69, oxalate, 112-15°; and I, NHBu, 71, oxalate, 98-102°. Me quinuclidine-3-carboxylate-HCl (2.1 g.) in 20 ml. 20% HCl was refluxed 15 hrs., dried, 15 ml. SOCl2 added, the mixture refluxed 3 hrs. and dried, 2.4 g. 2,6-Me2C6H3NH2 was added dropwise, 2.7 g. K2CO3 and 20 ml. CHCl3 were added, and the mixture refluxed 3 hrs. and worked up to give 60% II.HCl (R = 2,6-Me2C6H3NH, R1 = H), m. 236-8°. The following compds. were similarly prepared [compound type, R (or R and R1), % yield, salt, and m.p. salt given]: II, pyrrolidine, H, 48,-(free base), 99-100°; I, NMe2, 54, HCl, 180-2°; I, NEt2, 32, HCl, 168-70°; I, pyrrolidino, 39,-(free base), 87-8.5°; I, piperidino, 36, HCl, 183-4°; II, 2-MeC6H4NH, H, 55,-(free base), 169-70°; II, 2,6-MeClC6H3NH, H, 52, HCl, 226-8°; I, 2-MeC6H4NH, 49, HCl, 208-9°; I, 2,6-Me2C6H3NH, 45, HCl, 247-8°; and II, 2,6-MeClC6H3NH, 52, HCl, 236-7°. Ia was added to a solution of Na in the appropriate amino alc., and the mixture heated 6 hrs. at 70°/100 mm. to give the following II (R, R1, % yield, and m.p. given): O(CH2)2NMe2, OH, 73, 103-5°; O(CH2)2NEt2, OH, 73, 73-4.5°; pyrrolidinoethoxy, OH, 79, 90-1.5°; and piperidinoethoxy, OH, 82, 100-2°. III were prepared by treating the appropriate amino esters in Me2CO with MeI. The salt separated almost immediately and was collected and recrystd. from 90% EtOH. The following III were prepared (R, % yield, and m.p. given): NMe3, 95, 239-40°; NMeEt2, 92, 249-50°; N-methylpyrrolidino, 95, 247-8°; and N-methylpiperidino, 89, 248-9°. All the compds. were tested for pharmacol. and microbiol. activities, but showed no appreciable effects.

IT 23581-62-6P 23581-63-7P 23692-14-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 23581-62-6 CAPLUS

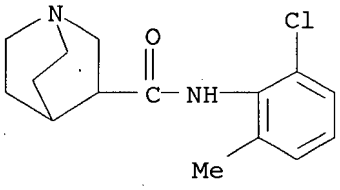
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2,6-dimethylphenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

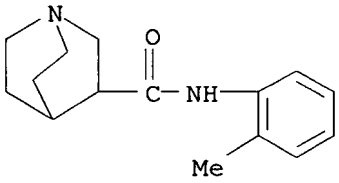
RN 23581-63-7 CAPLUS

CN [illegible] (CA INDEX NAME)



● HCl

RN 23692-14-0 CAPLUS
CN 1-Azabicyclo[2.2.2]octane-3-carboxamide, N-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 09:55:56 ON 14 MAY 2007)

FILE 'REGISTRY' ENTERED AT 09:56:11 ON 14 MAY 2007
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L2 3 S L1
L3 79 S L1 FULL

FILE 'CAPLUS' ENTERED AT 09:56:54 ON 14 MAY 2007
L4 13 S L3 FULL

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FULL ESTIMATED COST	69.45	241.76

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CA SUBSCRIBER PRICE	-10.14	-10.14

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(FILE 'HOME' ENTERED AT 09:55:56 ON 14 MAY 2007)

FILE 'REGISTRY' ENTERED AT 09:56:11 ON 14 MAY 2007
L1 STRUCTURE UPLOADED
L2 3 S L1

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L3            79 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 09:56:54 ON 14 MAY 2007
L4            13 S L3 FULL

     FILE 'STNGUIDE' ENTERED AT 09:58:02 ON 14 MAY 2007

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                    0.30     242.06

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CA SUBSCRIBER PRICE                                    0.00      -10.14

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NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13	FEB 26	MEDLINE reloaded with enhancements
NEWS 14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
NEWS 20	MAR 20	MARPAT now updated daily
NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 26	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 28	MAY 01	New CAS web site launched
NEWS 29	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 30	MAY 11	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS EXPRESS		NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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NEWS IPC8		For general information regarding STN implementation of IPC 8

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=> s nicotinic acetylcholine receptors
         37945 NICOTINIC
             1 NICOTINICS
         37946 NICOTINIC
                 (NICOTINIC OR NICOTINICS)
         75959 ACETYLCHOLINE
            72 ACETYLCHOLINES
         75979 ACETYLCHOLINE
                 (ACETYLCHOLINE OR ACETYLCHOLINES)
        641488 RECEPTORS
L1        3210 NICOTINIC ACETYLCHOLINE RECEPTORS
                 (NICOTINIC(W)ACETYLCHOLINE(W)RECEPTORS)

=> s l1 and memory?
        143306 MEMORY?
L2         159 L1 AND MEMORY?

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      22885320 PY<2003
L3           60 L2 AND PY<2003

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L3   ANSWER 1 OF 60  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:18847  CAPLUS
DOCUMENT NUMBER:          142:233395
TITLE:                    Multiple roles of cholinergic receptors in the
                          olfactory bulb-toward a unifying hypothesis
AUTHOR(S):                Carleton, A.; Castillo, P. E.; Vincent, J.-D.; Lledo,
                          P.-M.
CORPORATE SOURCE:         C.N.R.S., Institut de Neurobiologie Alfred Fessard,
```

Gif-sur-Yvette, 91198, Fr.
SOURCE: Recent Research Developments in Neurochemistry (2002), 5, 159-168
CODEN: RRDNFR
PUBLISHER: Research Signpost
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The main olfactory bulb is the 1st site of olfactory information processing in the brain. It constitutes a critical relay between the olfactory epithelium and the olfactory cortex. A remarkable feature of this structure is its massive innervation by cholinergic inputs from the basal forebrain. In this review, we discuss the functional interaction between cholinergic inputs and the intrinsic bulbar circuitry. To determine the roles of acetylcholine in the olfactory bulb, we first characterized the effects of cholinergic agonists on both neural excitability and synaptic transmission. The diversity of targeted bulbar neurons by cholinergic inputs and their multiple effects will be briefly presented. In particular, we present evidence that nicotinic acetylcholine receptors excite both output neurons of the bulb, mitral cells, as well as interneurons located in the periglomerular regions. Interestingly, nicotine-induced responses in interneurons are short-lasting, whereas responses in mitral cells are long-lasting which suggests different consequences upon their resp. firing properties. As found for nicotine-induced responses, activation of muscarinic receptors triggers opposite effects for interneurons and mitral cells; it inhibits the firing rate of interneurons from a deeper layer, the granule cells, while at the same time it increases the degree of GABA release onto mitral cells. Thus, cholinergic signaling has multiple and opposing roles in the olfactory bulb neuronal network. Together, the direct excitation of relay bulbar neurons and inhibition of granule cells allow the ascending cholinergic system to exert a powerful facilitating influence over the transfer of olfactory information from the bulb to the cerebral cortex. In turn, by increasing GABA release onto mitral cells, the activation of muscarinic receptors allows the synchronization of a cluster of output neurons sharing the same cholinergic innervation. These findings on the cholinergic control of olfactory bulb output to central structures may guide future studies linking neuromodulators to cortical memory formation.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:494146 CAPLUS
DOCUMENT NUMBER: 139:209108
TITLE: Effects of imidacloprid on the neural processes of memory in honey bees
AUTHOR(S): Armengaud, C.; Lambin, M.; Gauthier, M.
CORPORATE SOURCE: Laboratoire de Neurobiologie de l'Insecte, EA 3037, Universite Paul Sabatier Toulouse III, Toulouse, 31062, Fr.
SOURCE: Honey Bees: Estimating the Environmental Impact of Chemicals (2002), 85-100. Editor(s): Devillers, James; Pham-Delegue, Minh-Ha. Taylor & Francis Ltd.: London, UK.
CODEN: 69EDMA; ISBN: 0-415-27518-0
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The cholinergic system in insects is the main target of insecticides. One class of mols., the neonicotinoids, induces direct activation of the neuronal nicotinic acetylcholine receptors (nAChRs). In the honey bee these receptors are mainly distributed in the olfactory pathways that link sensory neurons to antennal lobes and mushroom bodies. These structures seem to play an important role in olfactory conditioning. The authors have previously shown that cholinergic antagonists injected in different parts of the brain impaired

the formation and retrieval of olfactory memory. The authors then advanced the hypothesis that, through the activation of the nAChR, the neonicotinoid imidacloprid (IMI) would lead to facilitation of the memory trace. To test this hypothesis, IMI was applied topically upon the thorax and the effects were tested on the habituation of the proboscis extension reflex induced by repeated sugar stimulation of the antennae. Animals treated with IMI to a dose that did not affect sensory or motor functions needed fewer trials than nontreated animals to show a reflex inhibition. This effect can be interpreted as a learning facilitation. The authors developed a functional histochem. of cytochrome oxidase (CO) to reveal the brain targets of the drug in the honey bee brain. Following IMI injection, a CO staining increase, probably linked to an increase in metabolism, was observed in the antennal lobes. In integrative structures, in particular the calyces of mushroom bodies, IMI exerted a facilitatory or inhibitory effect on neuronal metabolism depending on the dose. The brain targets of nicotinic ligands, including pesticides, can be compared by using this technique.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:121871 CAPLUS
DOCUMENT NUMBER: 139:223424
TITLE: Nicotinic cholinergic modulation: galantamine as a prototype
AUTHOR(S): Woodruff-Pak, Diana S.; Lander, Cynthia; Geerts, Hugo
CORPORATE SOURCE: Temple University and Albert Einstein Healthcare Network, Philadelphia, PA, USA
SOURCE: CNS Drug Reviews (2002), 8(4), 405-426
CODEN: CDREFB; ISSN: 1080-563X
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Nicotinic acetylcholine receptor pharmacol. is becoming increasingly important in the clin. symptomatol. of neurodegenerative diseases in general and of cognitive and behavioral aspects in particular. In addition, the concept of allosteric modulation of nicotinic acetylcholine receptors has become a research focus for the development of therapeutic agents. In this review the scientific evidence for changes in nicotinic acetylcholine receptors in Alzheimer's disease is described. Within this context, the pharmacol. of galantamine, a recently approved drug for cognition enhancement in Alzheimer's disease, is reviewed along with preclin. studies of its efficacy on learning and memory. Galantamine modestly inhibits acetylcholinesterase and has an allosteric potentiating ligand effect at nicotinic receptors. The data collected in this review suggest that the unique combination of acetylcholinesterase inhibition and nicotinic acetylcholine receptor modulation offers potentially significant benefits over acetylcholinesterase inhibition alone in facilitating acetylcholine neurotransmission.

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:966636 CAPLUS
DOCUMENT NUMBER: 138:219062
TITLE: Nicotinic receptors in circuit excitability and epilepsy
AUTHOR(S): Raggenbass, Mario; Bertrand, Daniel
CORPORATE SOURCE: Department of Physiology, University Medical Center, Geneva, CH-1211, Switz.
SOURCE: Journal of Neurobiology (2002), 53(4), 580-589
CODEN: JNEUBZ; ISSN: 0022-3034

PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

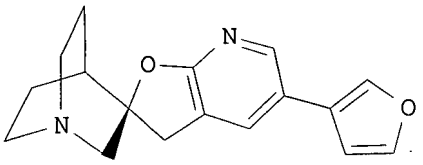
AB A review. Neuronal nicotinic acetylcholine receptors belong to the family of excitatory ligand-gated channels and result from the assembly of five subunits. Functional heteromeric nicotinic receptors are present in the hippocampus and neocortex, thalamus, mesolimbic dopamine system and brainstem motor nuclei, where they may play a role, resp., in memory, sensory processing, addiction and motor control. Some forms of autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) have been found to be associated with mutations in the genes coding for the α4 or β2 subunits of the nicotinic receptor. Mutant receptors display an increased acetylcholine sensitivity with respect to normal receptors. Since the thalamus and the cortex are strongly innervated by cholinergic neurons projecting from the brainstem and basal forebrain, an imbalance between excitation and inhibition, brought about by the presence of mutant receptors, could generate seizures by facilitating and synchronizing spontaneous oscillations in thalamo-cortical circuits.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:927434 CAPLUS
DOCUMENT NUMBER: 138:14045
TITLE: Preparation of (2'R)-5'-(3-furanyl)spiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine] as novel ligand for nicotinic acetylcholine receptors
INVENTOR(S): Phillips, Eifion
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096912	A1	20021205	WO 2002-SE1031	20020529 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455341	A1	20021205	CA 2002-2455341	20020529 <--
AU 2002303064	A1	20021209	AU 2002-303064	20020529 <--
EP 1397366	A1	20040317	EP 2002-731063	20020529
EP 1397366	B1	20070207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1512995	A	20040714	CN 2002-811049	20020529
BR 2002010075	A	20040817	BR 2002-10075	20020529
JP 2004532877	T	20041028	JP 2003-500091	20020529
NZ 529426	A	20050729	NZ 2002-529426	20020529
AT 353332	T	20070215	AT 2002-731063	20020529
ZA 2003008779	A	20050211	ZA 2003-8779	20031111
PRIORITY APPLN. INFO.:			US 2001-295206P P	20010601
			WO 2002-SE1031 W	20020529

GI



I

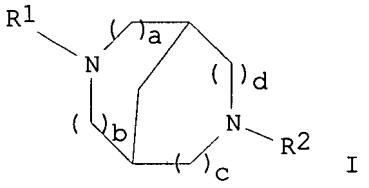
AB The title compound I.2HCl, useful in the treatment or prophylaxis of psychotic disorders or intellectual impairment disorders (no biol. data given), was prepared by bromination of (R)-spiro[1-azabicyclo[2.2.2]octane-3,2'(3'H)-furo[2,3-b]pyridine] followed by reacting the resulting 5'-bromo derivative with 3-furylboronic acid in the presence of Pd(PPh3)4 and Na2CO3 in H2O/EtOH/THF.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:927433 CAPLUS
DOCUMENT NUMBER: 138:14081
TITLE: Preparation of heteroaryl diazabicycloalkanes as central nervous system modulators
INVENTOR(S): Peters, Dan; Olsen, Gunnar M.; Nielsen, Elsebet Ostergaard; Ahring, Philip K.; Jorgensen, Tino Dyhring; Sloek, Frank Abildgaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002096911	A1	20021205	WO 2002-DK347		20020523 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002254880	A1	20021209	AU 2002-254880		20020523 <--
EP 1397365	A1	20040317	EP 2002-724151		20020523
EP 1397365	B1	20050216			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004538268	T	20041224	JP 2003-500090		20020523
AT 289310	T	20050315	AT 2002-724151		20020523
US 2004147505	A1	20040729	US 2003-479348		20031201
PRIORITY APPLN. INFO.:			DK 2001-866	A	20010601
			WO 2002-DK347	W	20020523

OTHER SOURCE(S): MARPAT 138:14081
GI



I

AB The present invention relates to novel diazabicycloalkanes (shown as I; a/b/c/d = 1,1,1,1, 1,1,1,2, 1,1,2,1, 0,2,0,2 and 0,0,2,2; see below for addnl. definitions of variables; e.g. 3-benzyl-7-(6-phenyl-3-pyridazinyl)-3,7-diazabicyclo[3.3.1]nonane), their labeled or unlabeled forms, any of their enantiomers, any mixture of enantiomers, or pharmaceutically acceptable salts thereof or a prodrug thereof, which are cholinergic ligands at the nicotinic acetylcholine receptors and modulators of the monoamine receptors and transporters. Due to their pharmacol. profile the compds. of the invention may be useful for the treatment of diseases or disorders as diverse as those related to the cholinergic system of the central nervous system (CNS), the peripheral nervous system (PNS), diseases or disorders related to smooth muscle contraction, endocrine diseases or disorders, diseases or disorders related to neuro-degeneration, diseases or disorders related to inflammation, pain, and withdrawal symptoms caused by the termination of abuse of chemical substances. A diazabicycloalkane derivative = those represented by Formula I, by Formula II, by Formula III, by Formula IV, and by Formula V. For I: n = 1, 2 or 3; R1 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkenylalkyl, alkynyl, alkynylalkyl, aryl, aralkyl or fluorescent group, which aryl groups may be substituted ≥1 times with substituents alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, methylenedioxy, hydroxy, alkoxy, alkoxyalkyl, alkoxyalkoxy, aryloxy, sulfhydryl, thioalkoxy, alkylcarbonyloxy, halogen, CF3, OCF3, CN, and nitro; and/or which aryl groups may be substituted with ≥1 fluorescent groups. R2 = a mono- or polycyclic aryl group, or a mono- or poly-heterocyclic group, which aryl and heterocyclic groups may be substituted ≥1 times with substituents alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, methylenedioxy, hydroxy, alkoxy, alkoxyalkyl, alkoxyalkoxy, aryloxy, sulfhydryl, thioalkoxy, alkylcarbonyloxy, halogen, CF3, OCF3, CN, and nitro; or which heterocyclic group may be substituted once with another mono- or poly-heterocyclic group, a mono- or polycyclic aryl group, or a mono- or polycyclic aralkyl group; and/or which heterocyclic group may be substituted with ≥1 fluorescent groups. Although the methods of preparation are not claimed, several example prepns. of I and intermediates are included and about 20 I are listed in the claims. Results for tabulated for two I regarding in vitro inhibition of 3H-5-Hydroxytryptamine (3H-5-HT, serotonin) uptake in cortical synaptosomes (e.g. IC50 = 0.022 μM for 3-benzyl-7-(2-quinolinyl)-3,7-diazabicyclo[3.3.1]nonane) and in vitro inhibition of 3H-cytisine binding (e.g. IC50 = 0.0030 for 7-(6-chloro-3-pyridazinyl)-3,7-diazabicyclo[3.3.1]nonane).

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:913864 CAPLUS

DOCUMENT NUMBER: 138:164983

TITLE: Chronic fluoride toxicity decreases the number of nicotinic acetylcholine receptors in rat brain

AUTHOR(S): Long, Yi-Guo; Wang, Ya-Nan; Chen, Jia; Jiang, Su-Fen; Nordberg, Agneta; Guan, Zhi-Zhong

CORPORATE SOURCE: China, Department of Pathology, Guiyang Medical College, Guiyang, Guizhou, 550004, Peop. Rep. China

SOURCE: Neurotoxicology and Teratology (2002), 24(6), 751-757
CODEN: NETEEC; ISSN: 0892-0362
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to investigate the mol. mechanism(s) underlying brain dysfunction caused by chronic fluorosis, neuronal nicotinic acetylcholine receptors (nAChRs) in the brain of rats receiving either 30 or 100 ppm fluoride in their drinking water for 7 mo were analyzed in the present study employing ligand binding and Western blotting. There was a significant reduction in the number of [3H]epibatidine binding sites in the brain of rats exposed to 100 ppm fluoride, but no alteration after exposure to 30 ppm. On the other hand, the number of [125I]α-BTX binding sites was significantly decreased in the brains of rats exposed to both levels of fluoride. Western blotting revealed that the level of the nAChR α4 subunit protein in the brains of rats was significantly lowered by exposure to 100 ppm, but not 30 ppm fluoride; whereas the expression of the α7 subunit protein was significantly decreased by both levels of exposure. In contrast, there was no significant change in the level of the β2 subunit protein in the brains of rats administered fluoride. Since nAChRs play major roles in cognitive processes such as learning and memory, the decrease in the number of nAChRs caused by fluoride toxicity may be an important factor in the mechanism of brain dysfunction in the disorder.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:839423 CAPLUS
DOCUMENT NUMBER: 139:94415
TITLE: The rationale behind cholinergic drug treatment for dementia related to cerebrovascular disease
AUTHOR(S): Grantham, C.; Geerts, H.
CORPORATE SOURCE: Janssen Research Foundation, Beerse, B-2340, Belg.
SOURCE: Journal of the Neurological Sciences (2002), 203-204, 131-136
CODEN: JNSCAG; ISSN: 0022-510X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Common to all subtypes of dementia, including Alzheimer's disease (AD), and those associated cerebrovascular disease (CVD), Lewy body pathol. and Parkinson's disease, is degeneration of cholinergic neurotransmission. The cholinergic hypothesis of AD is based on evidence of reduced cholinergic markers and decreased nos. of cholinergic neurons and nicotinic acetylcholine receptors (nAChR) in the hippocampus and cortex of the brain-both areas associated with memory, learning and executive function impairments characteristic of cognitive decline in AD. There is growing evidence for the involvement of the cholinergic system in vascular dementia (VaD). Attention has, therefore, recently turned to the use of cholinergic treatments such as galantamine (Reminyl), which has demonstrated broad-spectrum and long-term efficacy in AD, for the treatment of patients with VaD or AD with CVD. Galantamine is both a moderate, reversible, competitive acetylcholinesterase inhibitor, and an allosteric modulator of nAChR. Recent evidence suggests that the unmatched efficacy of galantamine in cognitive as well as behavioral and functional symptoms in patients with AD, as well as those with VaD or AD with CVD, may at least partly result from its unique dual cholinergic mode of action. Here, the rationale for using galantamine to treat dementia related to CVD is discussed. In particular, some interesting findings are covered which indicate the potential of galantamine to modulate other neurotransmitter systems (e.g. serotonergic, dopaminergic), which may be of specific relevance in the behavioral symptoms of dementia related to CVD.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:795369 CAPLUS
DOCUMENT NUMBER: 138:296914
TITLE: Preclinical experiments on cognition enhancement in Alzheimer's disease: drugs affecting nicotinic acetylcholine receptors
AUTHOR(S): Woodruff-Pak, Diana S.
CORPORATE SOURCE: Department of Psychology, Temple University, Philadelphia, PA, USA
SOURCE: Drug Development Research (2002), 56(3), 335-346
CODEN: DDREDK; ISSN: 0272-4391
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Nicotinic acetylcholine receptors (nAChRs) play a role in a variety of diseases of the central nervous system including Alzheimer's disease (AD). There is currently great interest in evaluating AD-related nAChR changes, and pharmacol. treatment of nAChR deficits is a promising therapy. In AD, α7 nAChRs remain relatively stable in contrast to α4β2 nAChRs that are lost in substantial nos. However, α7 nAChRs may be functionally impaired in AD because β-amyloid, a major neuropathol. in AD, blocks α4β2 and α7 nAChRs. Agonists selective to α7 or α4β2 nAChRs are neuroprotective against β-amyloid. A preclin. test of cognition-enhancing drugs affecting nAChRs is eyeblink classical conditioning. This task is severely impaired in human probable AD patients and is impaired by antagonists to nAChRs. Three drugs with different mechanisms of action on nAChRs (partial α7 nAChR agonism [GTS-21], acetylcholinesterase inhibition and allosteric modulation [galantamine], nootropic activation [nefiracetam]) were tested in young and older rabbits using eyeblink classical conditioning. All three drugs ameliorated learning and memory impairments in older rabbits and reversed an antagonist to nAChRs in young rabbits. Galantamine, with its allosteric modulatory action, was the only drug that facilitated learning in young rabbits. On the basis of efficacy of these drugs that affect nAChRs in preclin. studies and in Phase I (GTS-21), Phase II (nefiracetam), or Phase III (galantamine) clin. trials, exploration of nAChRs as targets for therapeutic intervention via a number of different pathways seems warranted.
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:739903 CAPLUS
DOCUMENT NUMBER: 138:297468
TITLE: Nonhalogenated anesthetic alkanes and perhalogenated nonimmobilizing alkanes inhibit α4β2 neuronal nicotinic acetylcholine receptors
AUTHOR(S): Raines, Douglas E.; Claycomb, Robert J.; Forman, Stuart A.
CORPORATE SOURCE: Departments of Anesthesia, Harvard Medical School, Boston, MA, USA
SOURCE: Anesthesia & Analgesia (Baltimore, MD, United States) (2002), 95(3), 573-577
CODEN: AACRAT; ISSN: 0003-2999
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nonhalogenated anesthetic alkanes, cyclopropane and butane, do not enhance γ-aminobutyric acid-elicited GABAergic currents, suggesting

that these agents produce anesthesia via interactions with other mol. targets. Perhalogenated nonimmobilizing alkanes; such as 1,2-dichlorohexafluorocyclobutane and 2,3-dichlorooctafluorobutane, also fail to enhance GABAergic currents, but display specific behavioral effects that are distinct from those of structurally similar anesthetics. At concns. predicted to be anesthetic, 1,2-dichlorohexafluorocyclobutane and 2,3-dichlorooctafluorobutane produce amnesia but fail to produce immobility. Neuronal nicotinic acetylcholine (nACh) receptors are sensitive to many anesthetics and are thought to have an important role in learning and memory. The authors postulated that neuronal nACh receptors might mediate the common amnestic action of nonhalogenated and perhalogenated alkanes. To test the hypothesis that neuronal nACh receptors have a role in mediating the behavioral effects of general anesthetics and nonimmobilizers, the authors quantified the inhibitory potencies of nonhalogenated anesthetic alkanes and perhalogenated nonimmobilizing alkanes on currents mediated by α4β2 neuronal nACh receptors. The authors' studies reveal that anesthetics and nonimmobilizers significantly inhibit α4β2 neuronal nACh receptors at concns. that suppress learning and with potencies that correlate with their hydrophobicities. These results support the hypothesis that α4β2 neuronal nACh receptors mediate the amnestic actions of alkanes but not their immobilizing actions.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:266265 CAPLUS

DOCUMENT NUMBER: 136:396280

TITLE: Nicotine preconditioning antagonizes activity-dependent caspase proteolysis of a glutamate receptor

AUTHOR(S): Meyer, Erin L.; Gahring, Lorise C.; Rogers, Scott W.

CORPORATE SOURCE: Salt Lake City Veterans Affairs-Geriatrics Research, Education, and Clinical Center and the University of Utah School of Medicine, Salt Lake City, UT, 84132, USA

SOURCE: Journal of Biological Chemistry (2002), 277(13), 10869-10875
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Neuronal excitation is required for normal brain function including processes of learning and memory, yet if this process becomes dysregulated there is reduced neurotransmission and possibly death through excitotoxicity. Nicotine, through interaction with neuronal nicotinic acetylcholine receptors, possesses the ability to modulate neurotransmitter systems through numerous mechanisms that define this critical balance. We examined the modulatory role of nicotine in primary mixed cortical neuronal-glial cultures on activity-dependent caspase cleavage of a glutamate receptor, GluR1. We find that GluR1, but not GluR2 or GluR3, is a substrate for agonist (α-amino-3-hydroxy-5-methyl-isoxazole-4-propionic acid)-initiated rapid proteolytic cleavage at aspartic acid 865 through the activation of caspase 8-like activity that is independent of membrane fusion and is not coincident with apoptosis. Dose-dependent nicotine preconditioning for 24 h antagonizes agonist-initiated caspase cleavage of GluR1 through a mechanism that is coincident with desensitization of both nAChRα4β2 and nAChRα7 receptors and the delayed activation of a caspase 8-like activity. The modulation of GluR1 agonist-initiated caspase-mediated cleavage by nicotine preconditioning offers a novel insight into how this agent can impart its numerous effects on the nervous system.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:127283 CAPLUS
DOCUMENT NUMBER: 136:395825
TITLE: Nicotine activates the extracellular signal-regulated kinase 1/2 via the α7 nicotinic acetylcholine receptor and protein kinase A, in SH-SY5Y cells and hippocampal neurones
AUTHOR(S): Dajas-Bailador, F. A.; Soliakov, L.; Wonnacott, S.
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, BA2 7AY, UK
SOURCE: Journal of Neurochemistry (2002), 80(3), 520-530
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neuronal nicotinic acetylcholine receptors (nAChR) can modulate many cellular mechanisms, such as cell survival and memory processing, which are also influenced by the serine/threonine protein kinases ERK1/2. In SH-SY5Y cells and hippocampal neurons, nicotine (100 μM) increased the activity of ERK1/2. This effect was Ca2+ dependent, and prevented by the α7 nAChR antagonist α-bungarotoxin (α-Bgt) and an inhibitor (PD98059) of the upstream kinase MEK. To determine the intervening steps linking Ca2+ entry to MEK-ERK1/2 activation, inhibitors of Ca2+-dependent kinases were deployed. In SH-SY5Y cells, selective blockers for PKC (Ro 31-8220), CaM kinase II (KN-62) or PI3 kinase (LY 294002) failed to inhibit the nicotine-evoked increase in ERK1/2 activity. In contrast, two structurally different inhibitors of PKA (KT 5720 and H-89) completely prevented the nicotine-dependent increase in ERK1/2 activity. Inhibition of the nicotine-evoked increase in ERK1/2 activity by H-89 was also observed in hippocampal cultures. Down stream of PKA, the activity of B-Raf was significantly decreased by nicotine in SH-SY5Y cells, as determined by direct measurement of MEK1 phosphorylation or in vitro kinase assays, whereas the modulation of MEK1 phosphorylation by Raf-1 tended to increase. Thus, this study provides evidence for a novel signaling route coupling the stimulation of α7 nAChR to the activation of ERK1/2, in a Ca2+ and PKA dependent manner.
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:106599 CAPLUS
DOCUMENT NUMBER: 136:177889
TITLE: Absence of α7-containing neuronal nicotinic acetylcholine receptors does not prevent nicotine-induced seizures
AUTHOR(S): Franceschini, Davide; Paylor, Richard; Broide, Ron; Salas, Ramiro; Bassetto, Laura; Gotti, Cecilia; De Biasi, Mariella
CORPORATE SOURCE: Division of Neuroscience, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Molecular Brain Research (2002), 98(1,2), 29-40
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nicotine is the primary addictive component in tobacco, and at relatively low doses it affects cardiovascular responses, locomotor activity, thermoregulation, learning, memory, and attention. At higher doses nicotine produces seizures. The mechanisms underlying the

convulsive effects of nicotine are not known, but studies conducted on a number of inbred strains of mice have indicated a pos. correlation between the number of α-bungarotoxin (α-BTX) binding sites in the hippocampus and the sensitivity to nicotine-induced seizures. Because α7-containing neuronal nicotinic acetylcholine receptors (nAChRs) represent the major binding site for α-BTX, mice lacking the α7 nAChR subunit were predicted to be less sensitive to the convulsive effects of nicotine. To test this hypothesis, we injected nicotine i.p. in α7 mutant mice and found that the dose-response curve for nicotine-induced seizures was similar in the α7 +/+, α7 +/- and α7 -/- mice. The retained sensitivity to the convulsant effects of nicotine could not be explained by the presence of cholinergic compensatory mechanisms such as increases in mRNA levels for other nAChR subunits, or changes in binding levels or affinity for nicotinic ligands such as epibatidine and nicotine. These findings indicate that α7 may not be necessary for the mechanisms underlying nicotine-induced seizures.

REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:38707 CAPLUS

DOCUMENT NUMBER: 136:178264

TITLE: Nicotinic acetylcholine receptor α7 and α4β2 subtypes differentially control GABAergic input to CA1 neurons in rat hippocampus

AUTHOR(S): Alkondon, Manickavasagom; Albuquerque, Edson X.

CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, 21201, USA

SOURCE: Journal of Neurophysiology (2001), 86(6), 3043-3055
CODEN: JONEA4; ISSN: 0022-3077

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The hippocampus, a limbic brain region involved in the encoding and retrieval of memory, has a well-defined structural network assembled from excitatory principal neurons and inhibitory interneurons. Because the GABAergic interneurons form synapses onto both pyramidal neurons and interneurons, the activation of nicotinic acetylcholine receptors (nAChRs) present on certain interneurons could induce either inhibition or disinhibition in the hippocampal circuitry. To understand the role of nAChRs in controlling synaptic transmission in the hippocampus, the authors evaluated the magnitude of nAChR-modulated GABAergic postsynaptic currents (PSCs) in pyramidal neurons and various interneurons of the CA1 region. Using whole cell patch-clamp recording and post hoc identification of neuronal types in rat hippocampal slices, the authors show that brief (12-s) nAChR activation by ACh (1 mM) or choline (10 mM) enhances the frequency of GABAergic PSCs in both pyramidal neurons and CA1 interneurons. The magnitude of α7 nAChR-mediated GABAergic inhibition, as assessed by the net charge of choline-induced PSCs, was highest in stratum lacunosum moleculare interneurons followed by pyramidal neurons and s. radiatum interneurons. In contrast, the magnitude of α4β2 nAChR-mediated GABAergic inhibition, as assessed by the difference between the net charge of PSCs induced by ACh and choline, was highest in pyramidal neurons followed by s. lacunosum moleculare and s. radiatum interneurons. The present results suggest that cholinergic cues transmitted via specific subtypes of nAChRs modify the synaptic function in the hippocampus by inducing a differential degree of GABAergic inhibition in the target neurons.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:38005 CAPLUS
DOCUMENT NUMBER: 137:4375
TITLE: Correlation of nicotinic receptor binding with clinical and neuropathological changes in Alzheimer's disease and dementia with Lewy bodies
AUTHOR(S): Sabbagh, M. N.; Reid, R. T.; Hansen, L. A.; Alford, M.; Thal, L. J.
CORPORATE SOURCE: Department of Neurosciences, UCSD, La Jolla, CA, USA
SOURCE: Journal of Neural Transmission (2001), 108(10), 1149-1157
CODEN: JNTRF3; ISSN: 1435-1463
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated the relationship between the loss of nicotinic acetylcholine receptors (nAChR) and the cognitive decline or neuropathol. changes seen in Alzheimer's Disease (AD) and dementia with Lewy bodies (DLB). Midfrontal (MF) cortex of 31 AD, 24 DLB and 11 non-demented controls was examined Total plaque (TP), neuritic plaque (NP) and neurofibrillary tangle (NFT) counts were obtained. NAChR binding was assayed using 3H-epibatidine [3H-EPI]. Last Blessed Information-Memory-Concentration scores (BIMC), Mini-Mental State Examination (MMSE), Mattis Dementia Rating Scale (DRS) scores were collected. There were no correlations between 3H-EPI binding and TP, NP, NFTs counts in either AD or DLB. Last BIMC, MMSE, DRS scores did not correlate with 3H-EPI binding in AD or DLB. Thus, decline in cognitive function does not correlate with loss of nAChR in DLB or AD at the end of life suggesting that later in these diseases, loss of nAChR binding is not a reliable marker of cognitive function in AD or DLB. Loss of nAChR activity does not appear to be related to plaques or NFTs in AD or DLB.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:711674 CAPLUS
DOCUMENT NUMBER: 136:63964
TITLE: SIB-1553A, (±)-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]thio}phenol hydrochloride, a subtype-selective ligand for nicotinic acetylcholine receptors with putative cognitive-enhancing properties: effects on working and reference memory performances in aged rodents and nonhuman primates
AUTHOR(S): Bontempi, Bruno; Whelan, Kevin T.; Risbrough, Victoria B.; Rao, Tadimeti S.; Buccafusco, Jerry J.; Lloyd, G. Kenneth; Menzaghi, Frederique
CORPORATE SOURCE: Merck Research Laboratories, La Jolla, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 299(1), 297-306
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Preclin. and clin. data have suggested the potential use of nicotinic acetylcholine receptor (nAChR) ligands for treating cognitive dysfunction associated with neurodegenerative diseases, such as Alzheimer's disease. SIB-1553A, (±)-4-{[2-(1-methyl-2-pyrrolidinyl)ethyl]thio}phenol hydrochloride, a novel nAChR ligand with predominant agonist subtype selectivity for β4 subunit-containing human neuronal nAChRs, was tested in a variety of cognitive paradigms in aged rodents and nonhuman primates after acute and repeated administration. S.c. administration of SIB-1553A improved delayed nonmatching to place performance in aged mice. In aged

rhesus monkeys, i.m. and oral administration of SIB-1553A improved choice accuracy in a delayed matching to sample task. SIB-1553A improved performances in these spatial and nonspatial working memory tasks but was less effective at improving performances in spatial reference memory tasks (i.e., aged rodents exposed to a discrimination task in a T-maze or trained to locate a hidden platform in a water maze). These data suggest that SIB-1553A has a predominant effect on attention/working memory processes. SIB-1553A also induced the release of acetylcholine in the hippocampus of aged rats and was equally effective whether administered acutely or repeatedly (6 wk of daily s.c. administration). Thus, rats repeatedly treated with SIB-1553A exhibit neither tolerance nor sensitization to the effects of the compound The SIB-1553A-induced cognitive improvement may be in part related to an increase in cholinergic function. The present study provides addnl. support for the use of subtype-selective nAChR ligands as a potential therapy for the symptomatic treatment of specific cognitive deficits (such as attention/working memory deficits) associated with aging and neurol. diseases.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:696995 CAPLUS

DOCUMENT NUMBER: 136:74

TITLE: Modulation of nicotinic receptor activity in the central nervous system: a novel approach to the treatment of Alzheimer disease

AUTHOR(S): Albuquerque, E. X.; Santos, M. D.; Alkondon, M.; Pereira, E. F. R.; Maelicke, A.

CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, 21201, USA

SOURCE: Alzheimer Disease and Associated Disorders (2001), 15(Suppl. 1), S19-S25
CODEN: ADADE2; ISSN: 0893-0341

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Impaired cholinergic function in the central nervous system is an early feature of Alzheimer disease (AD). Currently, cholinergic deficit is usually corrected by increasing the amount of acetylcholine in the synapse by inhibiting acetylcholinesterase (AChE). One of the most consistent cholinergic deficits in AD is the reduced expression of nicotinic acetylcholine receptors (nAChR) in the brain. Since these receptors are essential for learning and memory, restoring nicotinic cholinergic function is a promising approach to treating AD. Allosteric modulation of nAChR is a novel approach, which circumvents development of tolerance through long-term use of conventional nicotinic agonists. Allosteric modulators interact with receptor-binding sites distinct from those capable of recognizing the natural agonist. Pos. allosteric modulation of nAChR activity has no effect on conductance of single channels; instead, by facilitating channel opening, it potentiates responses evoked by the interaction of the natural agonist with presynaptic and postsynaptic nAChR. Allosteric modulation of nAChR activity could therefore potentially produce a significant benefit in AD. One such allosteric modulator is galantamine. In addition to increasing nAChR activity, galantamine also inhibits AChE. This novel, dual mechanism of action distinguishes galantamine from many other AChE inhibitors. Galantamine has been shown to improve cognitive and daily function for at least 6 mo in placebo-controlled trials, and to maintain these functions at baseline levels for at least 12 mo in a 6-mo open-label extension study. Galantamine has pos. effects on nAChR expression, which are likely to contribute to its sustained efficacy in the treatment of AD patients.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:556715 CAPLUS
DOCUMENT NUMBER: 135:236917
TITLE: Timing and location of nicotinic activity enhances or depresses hippocampal synaptic plasticity
AUTHOR(S): Ji, Daoyun; Lape, Remigijus; Dani, John A.
CORPORATE SOURCE: Division of Neuroscience and Structural and Computational Biology and Molecular Biophysics Program, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Neuron (2001), 31(1), 131-141
CODEN: NERNET; ISSN: 0896-6273
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study reveals mechanisms in the mouse hippocampus that may underlie nicotinic influences on attention, memory, and cognition. Induction of synaptic plasticity, arising via generally accepted mechanisms, is modulated by nicotinic acetylcholine receptors. Properly timed nicotinic activity at pyramidal neurons boosted the induction of long-term potentiation via presynaptic and postsynaptic pathways. On the other hand, nicotinic activity on interneurons inhibited nearby pyramidal neurons and thereby prevented or diminished the induction of synaptic potentiation. The synaptic modulation was dependent on the location and timing of the nicotinic activity. Loss of these synaptic mechanisms may contribute to the cognitive deficits experienced during Alzheimer's diseases, which is associated with a loss of cholinergic projections and with a decrease in the number of nicotinic receptors.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:549716 CAPLUS
DOCUMENT NUMBER: 136:273036
TITLE: Post-stroke dementia: Nootropic drug modulation of neuronal nicotinic acetylcholine receptors
AUTHOR(S): Zhao, Xilong; Yeh, Jay Z.; Narahashi, Toshio
CORPORATE SOURCE: Department of Molecular Pharmacology and Biological Chemistry, Northwestern University Medical School, Chicago, IL, 60611, USA
SOURCE: Annals of the New York Academy of Sciences (2001), 939(Neuroprotective Agents), 179-186
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nefiracetam is a new pyrrolidone nootropic drug that is being developed for clin. use in the treatment of post-stroke vascular-type and Alzheimer's-type dementia. Among a few neuroreceptors that have been identified as potential targets of nootropics, neuronal nicotinic acetylcholine receptors (nnAChRs) are deemed the most important since they are related to learning, memory, and Alzheimer's disease dementia. We have recently found potent stimulating action of nefiracetam on nnAChRs. Rat cortical neurons in long-term primary culture expressed nnAChRs. Whole-cell patch clamp expts. revealed two types of currents induced by ACh, α-bungarotoxin (α-BuTX)-sensitive, rapidly desensitizing, α7-type currents and α-BuTX-insensitive, slowly desensitizing, α4β2-type currents. Although α7-type currents were only weakly inhibited by nefiracetam, α4β2-type currents were potently and efficaciously potentiated by nefiracetam. Nefiracetam at 0.1 nM reversibly potentiated

ACh-induced currents to 200-300% of control. Very high concns. (about 10 μM) also potentiated these currents, but to a lesser extent, indicative of the bell-shaped dose-response relation known to occur for nefiracetam, even in animal behavior expts. Three specific inhibitors of each of PKA and PKC did not prevent nefiracetam from potentiating ACh-induced currents, indicating that these protein kinases are not involved in nefiracetam action. Pretreatment with pertussis toxin did not alter nefiracetam potentiation, indicating Gi/Go proteins are not involved. Pretreatment with cholera toxin did abolish nefiracetam potentiation. Thus, nefiracetam potentiation is mediated via Gs proteins. In conclusion, nefiracetam stimulates α4β2-type nnAChRs via Gs proteins at nanomolar concns. The potentiation of α4β2-type nnAChRs is thought to be at least partially responsible for cognitive enhancing action.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 60 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:436604 CAPLUS

DOCUMENT NUMBER: 135:178986

TITLE: β-Amyloid activates the mitogen-activated protein kinase cascade via hippocampal α7 nicotinic acetylcholine receptors: in vitro and in vivo mechanisms related to Alzheimer's disease

AUTHOR(S): Dineley, Kelly T.; Westerman, Marcus; Bui, Duy; Bell, Karen; Ashe, Karen Hsiao; Sweatt, J. David

CORPORATE SOURCE: Division of Neuroscience, Baylor College of Medicine, Houston, TX, 77030, USA

SOURCE: Journal of Neuroscience (2001), 21(12), 4125-4133
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Alzheimer's Disease (AD) is the most common of the senile dementias, the prevalence of which is increasing rapidly, with a projected 14 million affected worldwide by 2025. The signal transduction mechanisms that underlie the learning and memory derangements in AD are poorly understood. β-Amyloid (Aβ) peptides are elevated in brain tissue of AD patients and are the principal component of amyloid plaques, a major criterion for postmortem diagnosis of the disease. Using acute and organotypic hippocampal slice prepns., the authors demonstrate that Aβ peptide 1-42 (Aβ42) couples to the mitogen-activated protein kinase (MAPK) cascade via α7 nicotinic acetylcholine receptors (nAChRs). In vivo elevation of Aβ, such as that exhibited in an animal model for AD, leads to the upregulation of α7 nAChR protein. α7 NAChR upregulation occurs concomitantly with the downregulation of the 42 kDa isoform of extracellular signal-regulated kinase (ERK2) MAPK in hippocampi of aged animals. The phosphorylation state of a transcriptional mediator of long-term potentiation and a downstream target of the ERK MAPK cascade, the cAMP-regulatory element binding (CREB) protein, were affected also. These findings support the model that derangement of hippocampus signal transduction cascades in AD arises as a consequence of increased Aβ burden and chronic activation of the ERK MAPK cascade in an α7 nAChR-dependent manner that eventually leads to the downregulation of ERK2 MAPK and decreased phosphorylation of CREB protein.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3            60 S L2 AND PY<2003

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